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SOME PROBLEMS IN THE CYTODETECTION OF CERVICAL CARCINOMA *

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Were it not for the almost simultaneous development about twenty years ago of two novel concepts in the diagnosis of cancer, I should not have ridden down on a cold front from Minnesota to discuss with you the problem of smears in connection with anything other than infertility.

The first concept — and one that encountered early and bitter opposition—was the belief, championed by MacCarty, that cytologic changes rather than histologic architecture were the most important criteria in the diagnosis of malignant tumors. For this he was accorded the sobriquet of "One-cell MacCarty." In 1932, Broders described and gave the name "carcinoma in situ" to certain lesions of the skin, breast, colon, larynx and cervix that, although cytologically malignant, had not yet violated the basement membranes of their surfaces of origin. I should like to pay public tribute to these two investigators, since other workers, especially in the new field of cytology, have neglected somewhat to do so.

The second important concept, developed by Papanicolaou, embodied the principle that malignant tumors growing on a free surface, such as that of the cervix uteri, exfoliated some of their cellular constituents and that these elements could be identified as individual malignant cells by cytologic studies on secretions, smears, and scrapings from the part involved. Most important was the demonstration that material shed from the surfaces of in situ cancers was fully as diagnostic as that derived from advanced neoplasms.

DEVELOPMENT AND USES OF CYTOLOGIC DIAGNOSIS

The race for discovering early cancer then took on the aspects of a stampede. Every conceivable body orifice was swabbed, scraped, washed, siphoned, aspirated, brushed, and massaged for its maximal yield of cells, some of which might be malignant. Studies were conducted in which the efficacy of smears was compared with that of biopsy. The problem of "false positive" and "false negative" smears was the center of much discussion. The theoretic and actual relations between in situ cancers and clinical cancers were explored statistically and otherwise. Terms like "pre-cancer" and "nearo-cancer" were born in an attempt to explain the occurrence of "suspicious" smears of dubious cellular parentage. From a welter of literature on these and allied aspects of the problems posed

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by smears, two practical observations emerged, namely, (1) smears are extremely valuable in the detection of pulmonary or uterine cancer and (2) smears can be employed successfully in the discovery of almost 100 per cent of cervical cancer in its silent, invisible, eminently curable, in situ stage.

As surgeons and clinicians, you are all too familiar with the poor results of current attempts to cure obvious cancer of the cervix. Despite employment of the best methods available, the outlook is such that only about 1 woman in 5 who is suffering from this dread disease has a life expectancy of ten years. In the United States alone about 18,000 women, many of them young, die annually from its effects. If, by some simple office procedure, physicians could detect these malignant growths at a time when they can be cured by ordinary surgical technics like conization, they would indeed be achieving a signal victory in the fight against cancer. It is the conviction of many workers, based on substantial evidence, that this preclinical, invisible, and readily curable phase of cervical cancer lasts, on an average, for periods in excess of ten years. These in situ growths have been followed by design or by accident into the invasive and highly fatal form in such an imposing number of patients that to many investigators the sequence is inevitable. For the doubting Thomases, the fact remains that perhaps 5 per cent of cervical cancers which are discovered by smears prove, in spite of their invisibility, to be infiltrating growths at the time of conization or hysterectomy.

At this juncture, it might be well to ask this question: "Are not conventional methods of biopsy adequate for the detection of these early lesions?" By way of answer, I should like to cite the experience of my colleagues and myself at the Mayo Clinic. From 1932 to 1946, a total of 32 biopsies were done on carcinoma in situ of the cervix. Last year alone, our program of cervical smears uncovered no less than 95 examples of this lesion from a comparable cross section of clinic material. Currently, 5 of every 1,000 normal-appearing cervices prove cancerous when examined cytologically, and some of these contain growths that already are infiltrating.

Better-informed patients now know about this "new" test and often request it. To deny it to others perhaps is to neglect an extremely useful laboratory examination for cancer. So convinced are my associates and I of its importance that we are currently planning a threefold expansion of our facilities for its routine employment.

The detection of malignant tumors by study of smears is no longer an expensive program to be undertaken only in large university centers. It has been emphasized repeatedly that every doctor's office can be a cancer-detection center in which the making of cervical smears is an integral part of all routine pelvic examinations. Group participation by local medical and surgical societies in such cities as Toledo has established excellent patterns for pooling resources in such programs.

The problem, then, is one of detecting a high percentage of early cervical malignant growths at a stage when they are amenable to surgical treatment and in which a cure rate approaching 100 per cent can be achieved. Cancers of the uterine fundus are rarely asymptomatic; they occur in older women and their routine detection by curettage leads to a satisfactory rate of cure, since these lesions usually grow slowly. The early discovery of malignant tumors of the vulva, vagina, tubes, and ovaries likewise does not depend too much on study of smears.

PREPARATION AND STUDY OF CERVICAL SMEARS

I have chosen purposely to detail a method of making smears directly from the cervix rather than from the vaginal pool. Study of material from the latter source perhaps uncovers a few more endometrial growths than can be found in the former but it will fail in 10 to 20 per cent of cervical growths that do not exfoliate cells into the vagina. Two other advantages that are gained by obtaining

smears directly from the cervix are: (1) The concentration of malignant elements is always greatest at their source of supply and (2) the quality of cellular preservation is likewise improved by any method that yields "picked fruit rather than windfalls."

Role of the Clinician.—The following directions should be carefully observed by the clinician.

1. Do not use lubricant on the speculum, since the presence of extraneous matter on the smeared slide makes examination of the latter impossible. The speculum may be warmed and moistened by use of tap water.

2. Gently wipe excessive secretions from the external cervical os with a cotton applicator.

3. Using firm pressure, rotate the special wooden spatula around the external os, being certain to obtain scrapings from the squamocolumnar junction.

4. Smear the scrapings quickly and evenly on a glass slide and without a second's delay immerse the slide in a jar of fixative (95 per cent alcohol or ether-alcohol mixture). Under no circumstances permit the secretions to dry on the slide prior to fixation.

5. Label the slide and container accurately. If the slide is to be mailed out of town, allow fifteen to twenty minutes for fixation. If it is to be examined locally, transport it immersed in the fixative until it is ready for staining.

6. For maximal yield, make smears on all women more than 25 years of age and from those younger women who have abnormal-appearing cervices. Avoid taking smears while the patient is actively menstruating.

7. Do not biopsy the cervix at this time, and carefully unplug the office cautery.

Role of the Pathologist.—Three assumptions are necessary concerning the pathologist who now takes over; he must (1) believe in the entity of carcinoma in situ of the cervix, (2) be familiar with the interpretation of cytologic smears and (3) have help.

Each of these three items requires comment. It is utterly useless and twice as confusing to conduct a screening program designed to detect early cancer of the cervix if the tissue taken at biopsy from patients with positive smears is routinely diagnosed as "chronic cervicitis," "metaplasia," "basal cell hyperactivity" or other cant phrases. Smears made from in situ cancers contain cells that are indistinguishable from those which exfoliate from infiltrating growths. In situ cancers found by the smear technic should comprise from 90 to 100 per cent of the total, so it is prudent to be sure of the man behind the microscope.

With respect to the second item, the present requirements of the American Board of Pathology make it necessary that recently trained specialists in pathology be familiar with the interpretation of cytologic smears. Many of the older pathologists are conversant with the literature on the subject and are learning the technic through the medium of self-teaching. Short courses on exfoliative cytology are being conducted at a number of institutions, and the average pathologist attending such a course can become the key member of a screening team in a matter of weeks.

The problem of help for a busy pathologist is the biggest stumbling block in instituting these screening programs. Each cell in each smear must be viewed, a minimum of fifteen minutes being required to screen a single slide. The examination of two slides for each patient cuts in half the number of patients who can thus be studied. Examination of 25 smears per day per person approaches the maximum of visual endurance.

EXPECTED RESULTS OF A ROUTINE SCREENING PROGRAM

The use of trained technicians as cytologists provides the best solution to this bottleneck. After three months of special indoctrination, such technicians are each capable of staining and scanning smears at the rate of 5,000 per year. About 4,800 of these routine smears will be clearly negative. An additional 100 will con-

tain cells that the technician has marked and that will cost the pathologist many hours of toil and sweat before he gingerly consigns them to the negative category. There let them rest while the remaining 100 smears are considered.

This worrisome residue will be reported variously as being "positive" or "suspicious" for malignant cells. The task of uncovering the tissue source of these cells now goes back to the physician and his examining table. Employing Lugol's solution as an aid in defining the squamocolumnar junctional zone of the cervix, the physician removes from the cervix two to four pieces of tissue, which are cut deeply enough to insure proper orientation when they are embedded in paraffin. At this juncture, the office cautery is carefully put away in the cupboard, since to employ it in the arrest of minor bleeding is, in many instances, to destroy the very evidence of early carcinoma that the physician is trying so carefully to assemble. The fragments of tissue are placed in a small bottle containing a 10 per cent solution of formalin and are sent to the laboratory.

In perhaps 50 of these 100 worrisome cases, the pathologist within twenty-four hours reports the discovery of carcinoma, apparently in situ, in the material obtained at biopsy in the physician's office. In 25 additional cases, he may be satisfied that the presence of basal cell hyperactivity accounts adequately for what he has reported previously as "suspicious" cells. He may recommend that the patients in this group be followed, with repeated examination of smears at stated intervals. In the remaining 25 cases, he finds nothing at this stage to explain the "positive" smears.

The 75 patients whose cervices require further and immediate investigation are hospitalized for conization biopsy. This includes the 50 patients whose office biopsies disclosed cancer and the 25 in whom biopsy failed to reveal the source of the "positive" smears. Here, again, I must apologize for uttering a word of caution to the surgeon. Some of the cancers in this latter group of 25 patients are so small that they were missed during office biopsy. Too vigorous scrubbing of the cervix during the course of preoperative preparation of the vagina in the hospital may consign to the hamper of soiled linen the pinhead focus of cancer that gave rise to the worrisome cells found in the smear. Similarly, the performance of a useless and uninformative preliminary dilation and curettage has a crushing effect on delicate cells and a comparable one on the pathologist, who is seeking a generous cone of cervical tissue undisturbed by any preliminary maneuvers. The cone should extend from a base that is at least 5 mm. beyond the squamocolumnar junction to an apex at the endometrial cavity. It should be removed intact.

In our laboratory, because of the routine use of fresh frozen sections, we can cut, stain, mount, and examine material from 12 sections of these cones in as many minutes and report the findings to the surgeon. If the frozen-section technic is not available, it may be necessary to defer diagnosis for twenty-four hours or more until the material has been prepared by the paraffin method. In either instance, the pathologist may be expected to discover one or more foci of cervical cancer in the vast majority of cases. More than 90 per cent of the lesions will be in situ; thus, if conization of the cervix happens to be the surgeon's favored treatment, the patient will not need another operation. Some surgeons have had the experience of encountering recurrent carcinoma in situ after such minor sacrifice of tissue and, therefore, may elect to perform vaginal hysterectomy. From 5 to 10 per cent of the conized lesions will, surprisingly enough, reveal early carcinomatous infiltration, and the problem of radiation therapy versus radical hysterectomy will present itself. Residual neoplasm will not be detected in the surgically removed cone in perhaps 25 per cent of the cases in which the biopsy done in the office revealed carcinoma in situ. There are vari-

ous reasons for this; the tissue taken for biopsy included all the tumor, the cervix perhaps was touched with the cautery to control bleeding, the uterus was curetted prior to conization or the pathologist perhaps did not examine the cone thoroughly enough.

Finally, subsequent curettage is necessary for those patients in whom negative results were obtained on both biopsy and examination of the excised cone. This must be done in order to rule out the possibility of endometrial cancer before the smear is finally and sorrowfully classified in the categories of "false positive" or "false suspicious." It is a rare pathologist who does not harbor both these skeletons in his closet.

SUMMARY AND CONCLUSIONS

Routine study of cervical smears enables pathologists to detect an extremely high proportion of cervical cancers when they are in an asymptomatic, early, and eminently curable stage.

Incipient cancer of the uterine fundus, by contrast, gives warning symptoms. The making of smears from the vaginal pool for the detection of early fundal cancer is somewhat superfluous, and the method misses as many as 20 per cent of the more dangerous cervical lesions.

The pathologist who reports results of study of all cervical smears as either positive or negative is missing as many as 20 per cent of early lesions, which should have been discovered after they had been placed in a category labeled "suspicious cells present."

These early unsuspected lesions are extremely diminutive, and the hunt for them must be conducted as a co-operative venture, with observance of seemingly unimportant details.

POLIO IN CENTRAL LOUISIANA

THOMAS W. DAVIS, M. D.
ALEXANDRIA

The King Rand Polio Center, formerly The Mid-State Polio Center, was in continuous operation from June 1950 through December 1956. This center is unique in the state in that it was operated within the plant of a private hospital—Baptist Hospital, Alexandria—and was staffed totally by local physicians in private practice in the community. The program was financed by private gifts, by the local and National Polio Foundation, and at considerable financial expenditure by the Baptist Hospital over and above the grants. The staff also gave of their time for small financial remuneration. The Center was closed at the beginning of 1957, but is to be re-opened during polio epidemic season.

The purpose of this paper is to summarize some of the pertinent statistical data of the Center during this period and to investigate the unusually high incidence of polio in central Louisiana this past year in the face of an unusually low total U.S.A. incidence.

The majority of the patients of The King Rand Polio Center come from central and northeast Louisiana. The other two major centers at Shreveport and New Orleans are able to handle a greater number of patients than our Center, and in periods of peak admission patients were shunted from one center to another, depending upon bed space at the moment. Table 5 at the end of this paper shows the admissions by Parish in 1952 as compared to 1956.

TOTAL ADMISSIONS

Table 1 shows that 1125 patients were treated at the Center, 80 per cent being proved polio. There was a total of 35 deaths during that period. The rise in polio in 1956 over the three previous years is illustrated. The year 1950 would have shown a peak incidence, since the 183 admissions cover only seven months' operation in comparison to twelve months for the following years. It can be noted that there was no particular difference in the ratio of paralytic to nonparalytic during any of these years except the very low incidence in 1953. Nationally, the incidence of paralysis is about 40 to 45 per cent. A higher incidence of paralysis is common during the time of epidemics.[1]

* Presented at the regular monthly meeting of the Rapides Parish Medical Society, Alexandria, Louisiana, May 14, 1957.

The nonpolio cases were those admitted for suspected polio, and later proved to be other diseases. The final diagnosis on these cases was an amazing array of infirmities ranging from purulent meningitis, encephalitis, rheumatic fever, measles, tonsillitis, and even a fractured radius in one instance. This, of course, is largely nonpreventable in a center for acute cases receiving patients from a wide rural area. A large percentage of the patients had had no spinal tap or other laboratory work prior to admission. This is also true in other centers of similar type.[2] The diagnosis of abortive and presumptive polio is always dubious and gradually most of the staff members confined their diagnoses either to paralytic or nonparalytic polio, or "not polio". In computing national figures at present the Public Health Service has abandoned the latter diagnosis. The 35 deaths give a death rate of 3.9 per cent.

TABLE 1

Year	Admissions	Paralytic	Nonparalytic	Abortive Presumptive	Nonpolio
1950	183	87(52%)	50	9	37
1951	229	107(64%)	53	6	63
1952	184	72(51%)	64	1	47
1953	137	44(40%)	64		29
1954	138	67(56%)	41	9	21
1955	88	45(60%)	25	4	14
1956	166	76(56%)	59		31
Totals	1125	498(56%)	356	29	242

Deaths: 35 (3.9% total polio)
Total polio cases: 883

SEASONAL INCIDENCE

The seasonal incidence of admissions is comparable to the national rate and verifies the observation that polio is a summer disease. (Figure 1) We invariably had a rise in June and a rapid drop-off in September and October.

EFFECT OF VACCINE

The age distribution chart (Table 2) comparing admissions (polio only) in 1956 to 1951 was prepared in an effort to determine if vaccination programs had lowered the rate in the grammar school age groups. This group (age 6 to 12) in Rapides Parish was approximately 70 per cent inoculated by the spring of 1956. The differences are not statistically significant. This same type study done on a national basis, however, showed a definite drop in the incidence of the infection in the school age group.

TABLE 2
AGE DISTRIBUTION

	1951	1956
Less 1 year	9 (5%)	4 (3%)
1 "	19 (11%)	19 (15%)
2 "	16 (9%)	15 (11%)
3 "	11 (7%)	7 (6%)
4 "	19 (11%)	7 (6%)
5 "	16 (9%)	9 (7%)
6 to 10 "	40 (23%)	26 (20%)
11 to 15 "	22 (12%)	25 (19%)
16 to 20 "	12 (7%)	8 (6%)
Over 20 "	11 (6%)	8 (6%)

Table 3, which includes Rapides Parish figures only, shows a definite drop in the percentage of paralytic cases in those that previously received the vaccine. There were 13 cases of polio in the group that received inoculation, and only 4 showed any paralysis. This is significantly lower than the nonvaccinated groups. On a national scope it has been concluded that the vaccine not only lowers the infection rate but also definitely prevents the seriousness of the infection.[3]

VIRUS TYPE

Patients admitted to the center received a detailed laboratory survey which included stool cultures for virus and virus typing. This was done by the Section of

TABLE 3
POLIOMYELITIS CASES SHOWING VACCINATED STATUS, RAPIDES PARISH, 1956

	Total Cases	Vaccinated	Percent	Not Vaccinated	Percent
Total	61	13	21.3	48	78.7
Paralytic	31	4	12.9	27	87.1
Nonparalytic	30	9	30.0	21	70.0

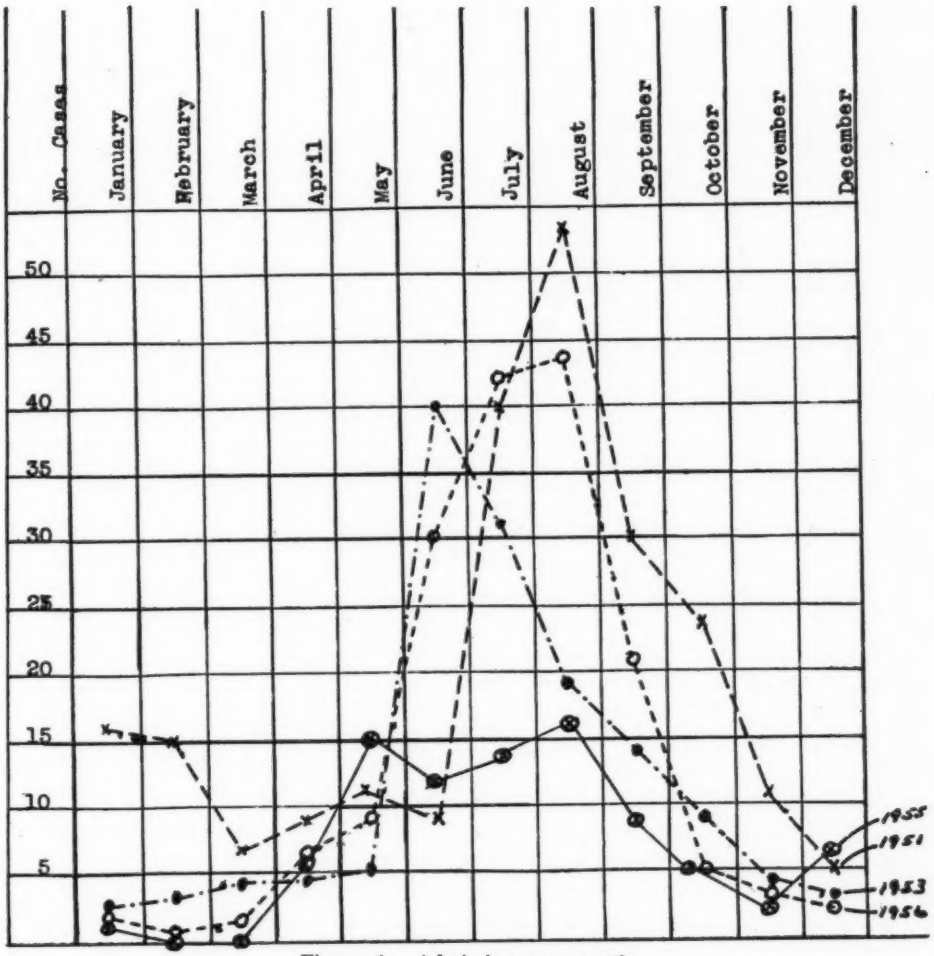

Figure 1.—Admissions per month.

Epidemiology of the State Department of Public Health under the direction of Dr. J. D. Martin. These records are incomplete as the studies were done 200 miles from the center and reports were frequently months in returning. Table 4 summarizes the return of cultures on 84 patients. As one might expect, there was a greater incidence of positive cultures in the more seriously ill patients. It was interesting that two cases diagnosed as "not polio" returned positive cultures.

Epidemiological centers have been typing polio virus since 1953, and gradually

TABLE 4
VIRUS DISTRIBUTION

Virus Type	Severe	Moderate	Slight	Nonparalytic	Total
I (Brunhelde)	20	11	6	8	45
III (Leon)	4	1		2	7
Negative culture		13		19	32
				Total	84

Note: 62% positive cultures
Two patients diagnosed as not polio had positive cultures, one Type I and one Type III

certain observations are becoming apparent.[4] It has been found that Type I (Brunhelde virus) is much the most frequent cause of serious epidemics, and that Type II (Lansing) and Type III (Leon) are responsible usually for the sporadic infections throughout the country. Only a few small outbreaks have been due to Type III. Generally speaking, Type I infections are accompanied by a greater amount of paralysis. This fact has been confirmed by our study.

It has been observed that many clinically diagnosed cases of nonparalytic polio have sterile stools and, in some cases, other virus such as Coxsackie or Echo are isolated. It is thus becoming apparent that many of our sterile meningitis cases showing meningismus and muscle spasm, but no paralysis, are not polio at all. This would possibly explain our large number of negative cultures in those cases.

In conclusion, I take the liberty of expressing the pride of our Society and the Baptist Hospital in the operation of the King Rand Polio Center over six and one-half years. A great deal of credit should go to the late Dr. King Rand for having the foresight and ability to organize and head the staff of this institution. It is by examples of this type of individual initiative and collective work of a local society that progress is made in medicine.

SUMMARY

1. Admissions to the King Rand Polio Center, Alexandria, for the past six and one-half years are reviewed.

2. Eleven hundred and twenty-five cases were admitted for treatment: 80 per cent proved to be polio, 56 per cent paralytic.

3. The vaccine appeared to reduce the incidence of paralysis in the few inoculated cases infected.

4. Virus studies as to types are recorded and discussed.

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TABLE 5
NUMBER OF ADMISSIONS

Parish	1952	1956	Parish	1952	1956
Rapides	39	71	Ouachita	22	2
Concordia	2	5	Evangeline	2	0
Avoyelles	36	24	Acadia	0	1
Grant	5	4	Red River	1	0
Allen	9	14	Jackson	0	1
Franklin	3	2	Union	9	0
Vernon	8	12	Washington	0	1
Madison	3	0	Richland	7	0
Catahoula	4	9	Beauregard	2	1
Caldwell	2	0	Cameron	1	0
LaSalle	4	7	Natchitoches	5	0
Sabine	2	0	Lincoln	2	0
Calcasieu	8	6	Morehouse	0	2
Lafayette	1	0	Winn	3	1
Jeff. Davis	1	0	St. Landry	1	2
			West Carroll	4	1

NATURAL INFECTION WITH POLIOMYELITIS VIRUSES AND OTHER ENTERIC VIRUSES OF MAN *†

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NEW ORLEANS

For the past four years we have been engaged in a study of the processes of natural transmission of, and immunization with polioviruses in a selected population in southern Louisiana. As a by-product of that study we have necessarily become interested in and have accumulated information concerning the natural occurrence of other enteric viruses of man. With the advent and widespread use of "Salk" poliomyelitis vaccine, the study was modified in January 1956, in order to determine the effect of this "killed-virus" vaccine on the transmission of polioviruses under natural conditions. Several reports have already been published [1-3] and others are now in press.[4-6] It is my purpose at this time to review briefly the results of that work, and to consider some of its implications to the physician in practice. Detailed presentations can be found in the previous publications. The results of similar studies in other parts of the country have recently been published,[7, 8] and are in general agreement.

METHODS

The study population was recruited during 1953, with the active cooperation of practicing physicians in all three areas and health unit personnel in the areas outside New Orleans. It finally consisted of 157 households, each of which included a newborn baby to serve as a known nonimmune index child. These families were divided as equally as possible into triad subgroups on the basis of area of residence, race and economic status, and family size. Three study areas were established: New Orleans as an urban area of relatively low prior poliomyelitis morbidity, Baton Rouge as an urban area of relatively high prior morbidity, and the semirural, so-called "Evangeline area" (Lafayette, Iberia, St. Mary's and St. Martin's Parishes) of low past incidence. The three socio-economic categories were designated as Negro, white-lower economic, and white-upper economic. Despite the effort to recruit households with a high probability of continuing cooperativeness and stability, inevitable losses occurred. The original 157 families in January 1954, which included 686 older associates and five co-twins in addition to the index babies, had declined to 136 households by December 1955, and when vaccination was offered in January 1956, 18 additional families withdrew leaving 118 under observation. During 1956, 8 more were lost, although 9 new, closely related families were admitted during the year and many additional babies were born into study households.

Upon admission to the study a record was started for each household which included pertinent medical and epidemiological information. This record was kept current by visits at least once each month by a public health nurse. At admission, an initial blood specimen was obtained from each household member, for the determination of poliovirus antibodies as a baseline. Thereafter, a blood specimen was collected annually to detect changes that might have occurred without the involvement of the index child. Until the reorientation of the study with vaccination in January 1956, blood and stool specimens were collected from each index child at monthly intervals. Following vaccination, routine bleedings were done only with reference to the vaccine inocula, but stool specimens were collected twice each month from all children under 15 years of age. In any case, the detection of infection in any child, as indicated by serological change or by virus isolation, was the signal for a special visit to the household for

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collection of clinical and epidemiologic information as well as blood and stool specimens from all family and other indicated associates. This made it possible to determine the extent of homologous primary infection in other previously nonimmune household members, and, less precisely, the extent of reinfection in those previously immune.

The laboratory methods have been described in detail elsewhere.[3] They consisted of standard and widely accepted methods utilizing in vitro tissue culture techniques for the detection of both fecal virus and serum neutralizing antibodies.

PATTERNS OF SERO-IMMUNITY TO POLIOMYELITIS IN THE STUDY POPULATION

It must be understood that the households included in this study do not constitute a random cross-sectional sample of the Louisiana population, but they are, however, representative of families with children in important population groups in southern Louisiana.

Examination of the initial sera collected in 1953 showed that sero-immunity to all three poliovirus types is abundantly present in the study areas, and is acquired at a comparatively early age. Figure 1 shows the age-specific percentages of immunity to each of the virus types in the study population. By school age an average of 69 per cent of individuals had acquired antibodies to any one virus type. The acquisition of sero-immunity to the three types appears to have proceeded at very nearly the same rate except for an apparent lag in Type 3 in young children. This suggested that infections with Type 3 virus had been less frequent in this area during several years prior to 1953, and that the relative deficiency in immunity to this type might set the stage for an epidemic of Type 3 infections during the next "polio season." As shown in Table 2, during 1954, Type 3 infections did predominate, occurring over three times as frequently as Type 1 infections. Figure 2 shows the reflection of this in the sero-immune patterns in the young child population. By January 1955, Type 1 sero-immunity was deficient as compared to Type 3, and during that year Type 1 infections predominated.

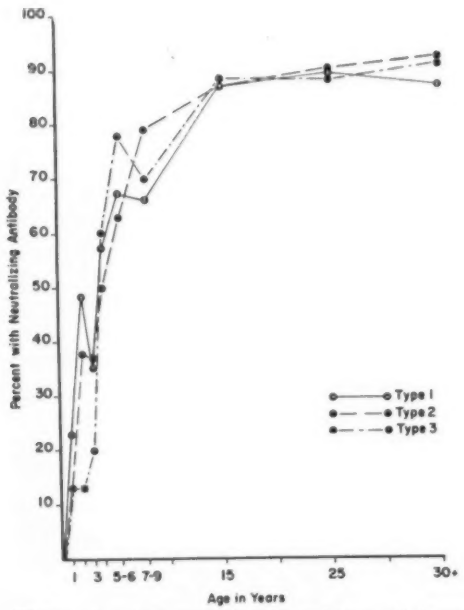

Figure 1.—Age-specific percentages of household associates of index children with neutralizing antibodies to types 1, 2, and 3 polioviruses when admitted to the study in 1953. (Reproduced with permission of the American Journal of Hygiene.[4]

To demonstrate differences in immunity patterns on the basis of race and economic status, average age-specific percentages were derived from the values for each of the three types. Figure 3 contrasts the pattern of sero-immunity in the three socio-economic groups. Overall the Negro group has the highest percentage of immunes (78 per cent) and the white-upper-economic group the lowest (64 per cent). During the two years that followed, the Negro group continued to acquire poliovirus infections and immunity at a faster rate than the white-upper group.

Differences in percentage of immunes between the three geographic areas did not become apparent until the three socio-economic groups were studied separately. Then it became evident that, although the Negro groups showed high percentages of immunes in all three communities, both white groups had significantly lower percentages in Baton Rouge than in either

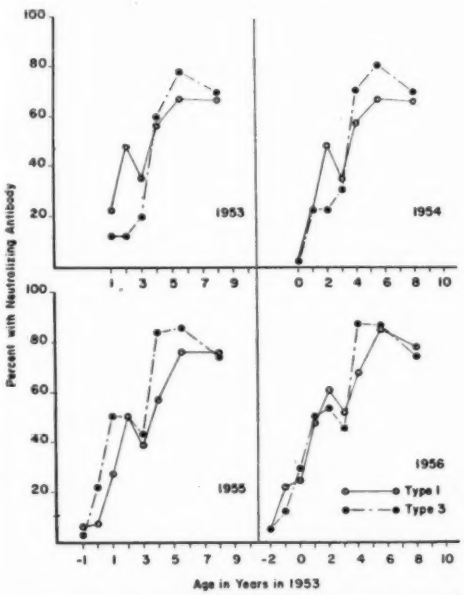

Figure 2.—Age-specific percentages of older siblings, original index children and their younger siblings § with neutralizing antibodies to types 1 and 3 polioviruses upon initiation of study in 1953 and at the beginning of the years 1954, 1955, and 1956, by years of age in 1953. (Reproduced with permission of the American Journal of Hygiene)[4]

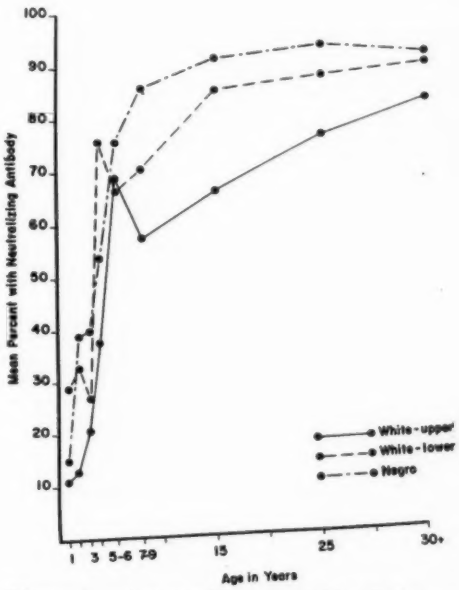

Figure 3.—Age-specific means ** of the percentages of older household associates †† with neutralizing antibody to each type of poliovirus upon admission to the study in 1953, by socio-economic or racial group. (Reproduced with permission of the American Journal of Hygiene)[4]

New Orleans or the Evangeline area. This is consistent with the relatively high past incidence of poliomyelitis disease in Baton Rouge.

POLIOVIRUS INFECTION EPISODES IN 1953-55 (BEFORE VACCINATION)

During an average of thirty months between the date of recruitment and January 1956, there were 114 household episodes of infection which involved an index child. These resulted in 253 primary infections of index children and their previously nonimmune household associates, and in the reinfection of at least 65 of their previously immune associates. Study of annual sera revealed 10 other abortive episodes which failed to involve the index baby but which caused an additional 24 primary infections.

Table 1 indicates for three complete years, 1954-1956, the seasonal distribution of those household episodes of infection which could be defined as to month of occurrence. Infections occurred in every month of the year, but with a marked peak in the summer.

When one examines the distribution of infection episodes by area during these three years of observation (Table 2), he is impressed with the absence of a consistent pattern. Each area experienced many episodes, but what occurred in any one gave little hint of what might be expected elsewhere, either in terms of the total number of infections or of the predominant virus type.

Race and economic status, as well as family size were important in determining the likelihood that poliovirus in-

§ Index children, born in 1953, do not figure in data until 1954; their younger siblings, born in 1954 and 1955, do not appear until 1955 and 1956, respectively. In this presentation maternally derived antibodies have been ignored.

** Mean value of the percentages with antibody to each of the three virus types.

†† Limited to persons still under observation as of January 1956, when final sera were collected.

fection would enter the home. In general, infections were more common in index children in the poorer environments of the Negro and lower economic white groups. They were also more frequent in households where two or more older siblings were present.

The age at which infections occurred in index babies gave no suggestion of periods of increased susceptibility. Infection was detected in one child only 23 days of age, and a total of 20 occurred during the first six months of life, four of the latter despite the demonstrated presence of maternally-derived passive antibody.

The examination of specimens collected on special visits made to the households following infection of an index child and the examination of annual sera, made it possible to show, as in Table 3, the primary infections that occurred in all homologously nonimmune individuals, including index babies, when any one person became infected in the home. It is evident that intrafamilial spread of poliovirus infection is the rule, particularly among children. Less than 10 per cent of susceptible children escaped infection, and for some of these an explanation was readily available, such as protracted absence from the home or unusual isolation from other family members. Not indicated in the table is the fact that many of the "missed" children were babes-in-arms whose exposure opportunities may have been reduced. A greater percentage of adults missed infection, probably also related to the lesser likelihood of fecal contamination.

Reinfection of homologously immune household associates was proved either serologically or by virus isolation in 21 per cent of such individuals. This is a minimal figure—an estimate, based on indirect evidence, of at least 50 per cent is probably closer to the truth. However, fecal virus was much less frequently detected in reinfected persons (about 7 per cent) than in those undergoing primary infection (about 42 per cent).

Suggestive evidence was obtained for spread between adjacent households and within the neighborhood. Direct, frequent, play contact between two or more households within our study group was established in relation to 7 infection episodes. Infections were detected simultaneously in the associated households in 3 instances, and in another 3 instances it followed in the related household one month later.

TABLE 1
MONTHLY DISTRIBUTION OF EPISODES OF HOUSEHOLD INFECTION WITH POLIOVIRUSES IN SOUTHERN LOUISIANA IN 1954-1955, BEFORE VACCINATION, AND IN 1956, AFTER TWO INOCULATIONS OF "SALK" VACCINE

Year	Number of Episodes in Month Indicated												
	J	F	M	A	M	J	J	A	S	O	N	D	Total
1954	0	0	1	0	3	7	19	6	7	10	2	2	57
1955	5	0	3	4	3	4	8	12	3	0	3	3	48
1956	0	2	2	3	5	10	8	8	2	5	0	0	45
Total	5	2	6	7	11	21	35	26	12	15	5	5	150

TABLE 2
DISTRIBUTION OF EPISODES OF HOUSEHOLD INFECTION WITH POLIOVIRUSES IN SOUTHERN LOUISIANA BY AREA, YEAR, AND VIRUS TYPE IN 1954-1955, BEFORE VACCINATION, AND IN 1956, AFTER TWO INOCULATIONS OF "SALK" VACCINE

Area	Number of Infections of Indicated Type in the Year:															
	1954				1955				1956				Total			
	1	2	3	Total	1	2	3	Total	1	2	3	Total	1	2	3	Total
New Orleans	7	4	9	20	12	4	2	18	5	0	3	8	24	8	14	46
Baton Rouge	1	6	11	18	7	11	0	18	3	4	4	11	11	21	15	47
Evangeline	0	10	9	19	6	0	6	12	20	0	6	26	26	10	21	57
Total	8	20	29	57	25	15	8	48	28	4	13	45	61	39	50	150

TABLE 3
PROVED INFECTIONS IN PREVIOUSLY NON-IMMUNE INDIVIDUALS RESIDENT IN HOUSEHOLDS UNDERGOING EPISODES OF POLIOVIRUS INFECTION IN 1953-1955, BEFORE VACCINATION, AND IN 1956, AFTER TWO INOCULATIONS OF "SALK" VACCINE*

Category of Person	Infections Occurring in the Indicated Year					
	1953-1955			1956		
	Number of Persons Susceptible	Infected		Number of Persons Susceptible	Infected	
		Number	Per Cent		Number	Per Cent
Adult	23	15	65	6	2	33
Child	284	262	92	95	87	92
Total	307	277	90	101	89	88

* Including households with "abortive" episodes in which the index child escaped infection.

Only in one did the related household escape infection entirely. In several episodes study group households had no direct contact but were located at varying distances from each other in the same neighborhood. Here also, infection was usually found in both houses, either simultaneously or at intervals up to two months.

It was usually not possible to follow the chronology of infection within a given household, but several fortuitous observations permit the general statement that infection apparently* is introduced into the home by a child of pre-school or early school age. From him, infection spreads almost simultaneously to all other non-immune members of the family.

Clinical histories, taken shortly after the infection episodes were detected, revealed no illness in relation to 72 per cent of the primary infections. Minor febrile illness at an appropriate time was recorded for 24 per cent of such persons, and in 9 instances (4 per cent) minimal aseptic meningitis was suggested in retrospect. There were no cases of paralytic disease. The ratio of overt poliomyelitis to poliovirus infections, estimated very crudely by comparing the calculated number of infections in the entire population of Louisiana in 1954 and 1955 with the number of cases reported in those years, was approximately 800 infections for every one diagnosed case.

POLIOVIRUS INFECTION EPISODES IN 1956 (FOLLOWING VACCINATION)

In January and February 1956, using "Salk" vaccine of a single lot and kindly provided by the Louisiana State Department of Health, a 2-dose primary course of vaccine was given to all children in study group households below the age of 15 years who did not already possess antibodies to all three types of poliovirus. No ill effects were noted as a result of vaccination.

The response to vaccination in children who were immunologically inexperienced or only partially experienced with poliovirus from prior infection is shown in Table 4. Two important facts are immediately evident; there was a marked

TABLE 4
APPEARANCE OF NEUTRALIZING ANTIBODY ONE MONTH AFTER TWO INOCULATIONS OF "SALK" POLIOMYELITIS VACCINE

Number inoculated	Pre-vaccination immunity	Post-vaccination Immunity-per cent of Inoculated Children Responding to Indicated Type								
		Type 1			Type 2			Type 3		
		No response	Low* Titer	High† Titer	No response	Low Titer	High Titer	No response	Low Titer	High Titer
118	None	36	30	34	26	21	53	60	23	18
94 - 97	Heterologous ‡	10	22	68	8	14	77	18	32	50

* Titer less than 1:10
† Titer 1:10 or greater
‡ Persons immune to one or two virus types. Response is shown only to the type or types not present prior to vaccination.

difference in antigenic potency between types, type 2 being the most effective and type 3 the least, and response to vaccination for any individual type was greater in children who had had some previous natural experience with other poliovirus types. Nevertheless, even in the latter group there was a significant proportion of children who had no detectable response, although it must be remembered that only the primary course of two inoculations had been given. Incomplete results of tests for neutralizing antibody following the third or booster inoculum, given in January 1957, show that with very few exceptions, these children had had a satisfactory priming stimulus, and were responding to the third "shot" with readily detectable antibody in high titer.

In 1956, there were 47 episodes of natural infection among the 118 households remaining under observation. Two of these were in single individuals undergoing reinfection and would not have been detected by the methods used from 1953 through 1955. The remaining 45 episodes are comparable, and it is evident that vaccination did not reduce the frequency of household infections. The monthly distribution of infections (Table 1) was also not altered, and the pattern of household episodes with the three types in the three study areas (Table 2), remained sporadic and difficult to interpret.

Perhaps of greatest interest is the extent of intra-household spread after virus is introduced, and Table 3 compares this phenomenon before and after vaccination. Among the children, there was no difference whatsoever, and between the small groups of adults the difference had no statistical significance. Table 5 helps to show why this was so. The duration of fecal virus excretion by infected children who were vaccinated but who had no prior infection immunity (forty-four days) was essentially as long as that by unvaccinated children (fifty-one days). The duration of excretion by naturally immune, reinfected persons was much shorter (twenty-two days). In addition to the duration of excretion, the quantity of virus excreted was studied, and the mean titer of virus in the first positive stool specimen from vaccinated and unvaccinated children was exactly the same.

INFECTIONS WITH OTHER HUMAN ENTERIC VIRUSES

Knowledge concerning enteric virus infections in man, other than poliovirus, is of very recent origin and is accumulating at a rapid rate at the present time. These agents were first encountered in 1948 as incidental findings in the feces of poliomyelitis patients. Their discovery stimulated a great deal of interest, at first because of their possible relationship to poliomyelitis, and more recently because of their defined role in the production of other disease syndromes.

Many viruses which are probably only passengers from loci of infection in the throat and respiratory system, e.g. adenoviruses, mumps, influenza, and herpes simplex may be found on occasion in human feces. Two other groups are recognized as primarily enteric in nature, the Coxsackie viruses [9] and the orphan or ECHO (enteric cytopathogenic human orphan) viruses.[10] The agent of infectious hepatitis is almost certainly also a true enteric pathogen, but it has not been positively identified.

Both the Coxsackie and ECHO groups

TABLE 5
DURATION OF FECAL POLIOVIRUS EXCRETION IN CHILDREN INFECTED IN 1954-1955, BEFORE VACCINATION, AND IN 1956, AFTER TWO INOCULATIONS OF "SALK" VACCINE

Previous Immunity Status	1954-1955				1956			
	Number excreting virus	Days duration			Number excreting virus	Days duration		
		Observed		Estimated true mean		Observed		Estimated true mean
		Range	Mean			Range	Mean	
Non-immune	110	1-114	24	51	84	1-105	26	44
Immune	—	—	—	—	16	1-43	7	22

have been incriminated as the etiological agents of human disease. Epidemic pleurodynia, aseptic meningitis, myocarditis of the newborn, herpangina, and "summer grippe" are believed to be possible manifestations of Coxsackie virus infection.[11, 12] Aseptic meningitis has been associated with ECHO viruses,[13] and some diarrheal syndromes may be the result of infection with these or similar agents.[14] However, in both groups the individual antigenic types differ in their pathogenicity; some types may never, or only rarely, cause disease.

Our contribution to this subject has been the demonstration of the ubiquity of enteric virus infections in this area.[6] Previously, fecal surveys in Cincinnati and in Mexico City and Vera Cruz, Mexico[15] and a longitudinal study over two years' time in Winston-Salem [16] had shown the frequency with which young children are infected. Based on the stool specimens obtained for the detection of poliovirus infection in our index children, it was also possible to show the enteric viral burden of these healthy children in southern Louisiana. Figure 4 represents a summary of the monthly percentages of virus isolations over a two-year period, 1954-1955. The viruses have been divided into only two categories: polioviruses (including all three types) and non-polio viruses. The

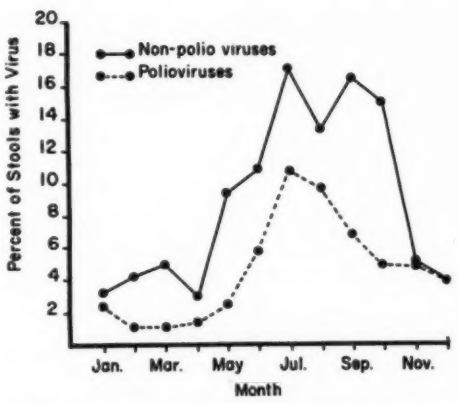

Figure 4.—Mean monthly percentages of stool specimens from healthy children in southern Louisiana found to contain polioviruses and other enteric viruses, 1954-1955.

latter are being studied in our laboratory now by Dr. Wolf Henigst. Preliminary results indicate that about 25 per cent are Coxsackie types, 25 per cent are ECHO types, and the remaining 50 per cent are still unidentified.

It is evident that enteric viruses are being excreted throughout the year in this area, and with peaks in the summer and autumn months. For the total index child group, infections reached a maximum of 29.9 per cent in July 1954. Smaller segments of the population gave even higher percentages; for the New Orleans group only, it was 38 per cent in September 1955, and for the Negro part of the group in that month was 64 per cent.

The effect of socio-economic status was demonstrable; both virus groups were found with greatest frequency in the Negro and least often in the white-upper economic populations. Family size did not show a demonstrable effect. Although not studied in detail, the non-polio viruses also tended to occur in family episodes, and such episodes tended to be confined to the younger members of the family. Epidemiologically these agents will probably be demonstrated to behave in a manner very similar to the polioviruses.

DISCUSSION

We believe that the data accumulated during the course of this and similar studies help to provide a rational basis for the management of the patient and the community in the prevention of poliomyelitis and other diseases which result from enteric virus infection. Some of the conclusions to be derived from this work will appear negative in the sense that they suggest that action not be taken. However, in the handling of a disease with the emotional overtones of poliomyelitis, moderation and restraint may be helpful suggestions.

Fundamental concepts which we believe have been demonstrated are as follows. Human enteric viruses are almost ubiquitous, and infection with polioviruses, and probably many others of the enteric group, are essentially inevitable during any nor-

mal lifetime. The degree to which different populations are saturated with these viruses undoubtedly varies, but southern Louisiana is a highly endemic area. Within any locality, the intensity of infection varies with socio-economic status (related to inter- and intra-household crowding, level of personal hygiene, etc.), and in descending order of the frequency of infection here are the Negro, white-lower economic, and white-upper-economic segments of the population. Polioviruses of all three types are usually present in the community, the predominant type being determined by the number of children nonimmune to each. Finally, these viruses are circulating throughout the year, but are much more abundantly present during the summer and autumn months, perhaps due to the greater frequency of intimate play contact among lightly clad young children during the warmer part of the year.

Within the community, polioviruses are probably spread primarily in a horizontal manner through the pre-school child population. This is suggested because: (1) the majority of the population is serologically immune by school age. (2) Immune individuals, even if reinfected, are less effective shedders of virus. (3) Young children have the lowest hygienic standards within any given socio-economic class and thus provide the most effective cohort for spread. (4) In the few instances where we were able to define the individual responsible for bringing the virus into the household, it was a child of this age. After virus is within the home, secondary spread in a vertical manner to older and younger associates not yet immune to the specific type occurs rapidly because of the greater intimacy of contact between family members.

A primary course of two inoculations of poliomyelitis vaccine of the "killed" type ("Salk vaccine") may well be of real value in preventing disease in the individual,[17] but it has no effect in reducing infection and transmission. This is very reassuring since it permits the continuing process of natural immunization before the potential "wearing-off" of vaccination immunity over the years. The phenomenon suggests, however, that oral vaccination with living, attenuated poliovirus strains, which more closely reproduces the natural process and which may result in life-long protection, is desirable. Neither vaccine, however, could have even a prophylactic effect if given to a family after demonstrated illness in a member because by the time illness is recognized all previously nonimmune individuals have already been infected. Even in a community the effectiveness of vaccine in stopping an epidemic may be limited because of the widespread infection that has already occurred by the time the epidemic is recognized. For vaccine to be maximally effective, therefore, it should be administered before the need becomes apparent.

Measures other than vaccination for community protection from poliomyelitis are limited. Infection is occurring constantly—perhaps we should say immunization, to accent the positive—and as long as it is subclinical, should be aided rather than hindered. Disease in the individual probably results both from personal factors, such as fatigue, provocative inoculations, tonsillectomy, and the age at which infection occurs, and from the relative virulence of virus strains. Since virus excretion is both prolonged in the individual and widespread in the community, personal and public quarantines are not likely to be very helpful. During a sharp epidemic, in which an unusually virulent strain can be presumed to be circulating, the limitation of large gatherings of children may be considered, but if it is, it must be evaluated in terms of the opportunity such gatherings provide for intimate contact, and a church picnic may be more dangerous than the oft-condemned swimming pool. Personal recommendations by the family physician for the avoidance of excessive fatigue and of unnecessary inoculations, prompt bed rest for suspicious summertime illnesses, and early prophylactic vaccination remain the most useful

preventive measures.

SUMMARY

A group of families in New Orleans, Baton Rouge and 4 semi-rural parishes in south Louisiana, of differing socio-economic status and differing size, have been under observation since 1953 in a study of the natural transmission of enteric viruses. Based on serological evidence in associates of the newborn index child in each household, the pattern of immunity to poliomyelitis in this area was determined. It indicated the early acquisition of antibodies to all 3 poliovirus types as well as differences related to socio-economic status and family size. One hundred and twenty-four episodes of household infection with polioviruses were found prior to "Salk" vaccination in January 1956, and 47 following vaccination. Infections occurred throughout the year, but most commonly in the summer, and in individuals of all ages. Spread of virus through the family and the community was observed, and the ease with which transmission occurs was noted. A primary course of two inoculations of "Salk" vaccine was given to all nonimmune children early in 1956, and vaccination was found not to change the pattern of infection and transmission in any significant manner during the following year. The ubiquity of infections with enteric viruses other than those of poliomyelitis was demonstrated, and their occurrence compared with the polioviruses. Finally, the implications of these findings to the practicing physician in the prevention of disease resulting from enteric virus infection was discussed.

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HOSPITAL FACILITIES IN LOUISIANA, 1953

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In order that physicians of Louisiana may readily acquaint themselves with some of the facts concerning hospital fa-

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cilities in their state and particularly with how these facilities compare with those of other states, a series of maps and charts has been prepared from data in the hospital supplement of *The Journal of the American Medical Association* for 1954.[1] While these data do not reflect the recent developments, the general situation has not been drastically altered. These illustrations give convincing evidence that hospital services in this state, considered as a whole, occupy an advantageous position in the Southern Region and, indeed, make a relatively favorable showing in the entire nation.

In the first pictorial presentations, Figures 1 and 2, volumetric symbols

Figure 1

(spheres) are used to indicate numbers of general hospital beds. The location of private hospitals, as depicted in Figure 1, generally follows population distribution, providing a more uniform coverage of the state than do state hospitals, shown in the next figure. Note the larger spheres representing the larger hospitals in New Orleans, Baton Rouge, Alexandria, and Shreveport. The populous Southern part of the state maintains more of the smaller individual hospitals which primarily provide general hospital beds. There are 8,040 private general hospital beds in Louisiana.

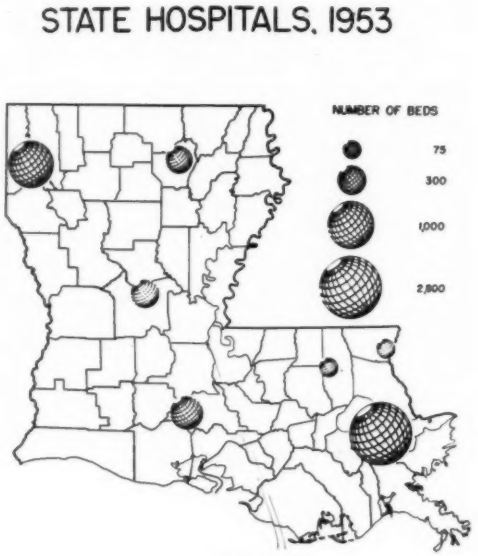

Figure 2

Figure 2 depicts the general hospitals of the state system in 1953, which are: Charity Hospital in New Orleans, Lallie Kemp in Independence, Washington and St. Tammany Charity Hospital in Bogalusa, Lafayette Charity Hospital, Huey P. Long Hospital in Pineville, E. A. Conway Memorial Hospital in Monroe, and Confederate Memorial Hospital in Shreveport. In Louisiana virtually all public medical care is furnished by the state at no direct cost to the patient. In 1953 there were 4,804 general hospital beds in these state hospitals.

Figure 3 shows the comparative standing of Louisiana and other states in the category of all general hospital beds, both private and public types. Louisiana is considerably better supplied with these hospital beds than other Southern States, and it ranks with the states of New York, Pennsylvania, California, Wisconsin, and others in this category of hospital beds.

Figure 4 presents local and state governmental hospital beds of all types, including mental hospitals. Again, in this comparison, Louisiana outranks the other

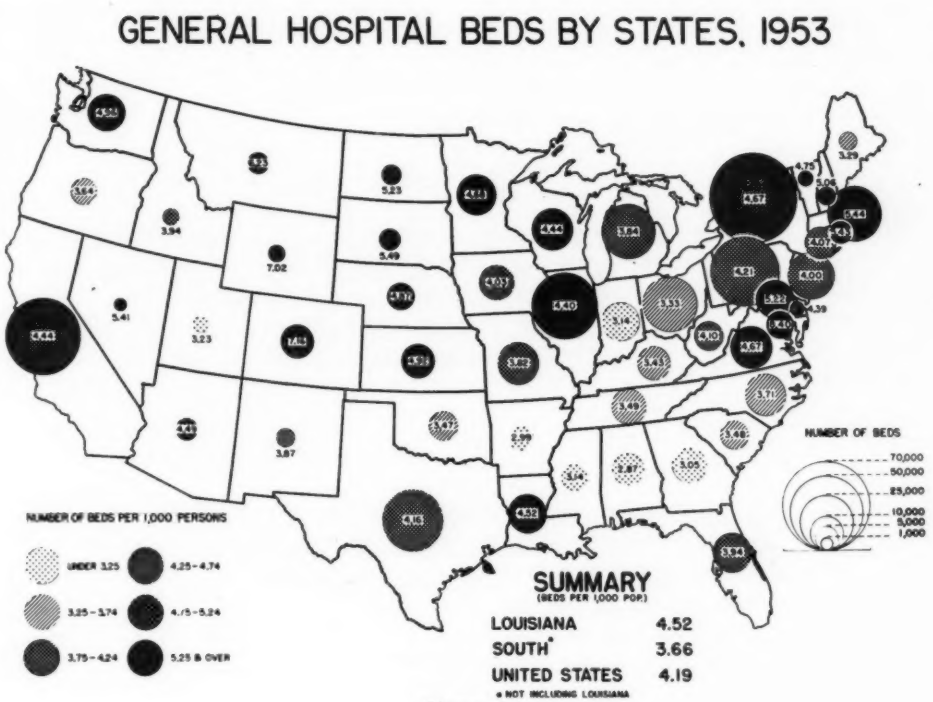

Figure 3

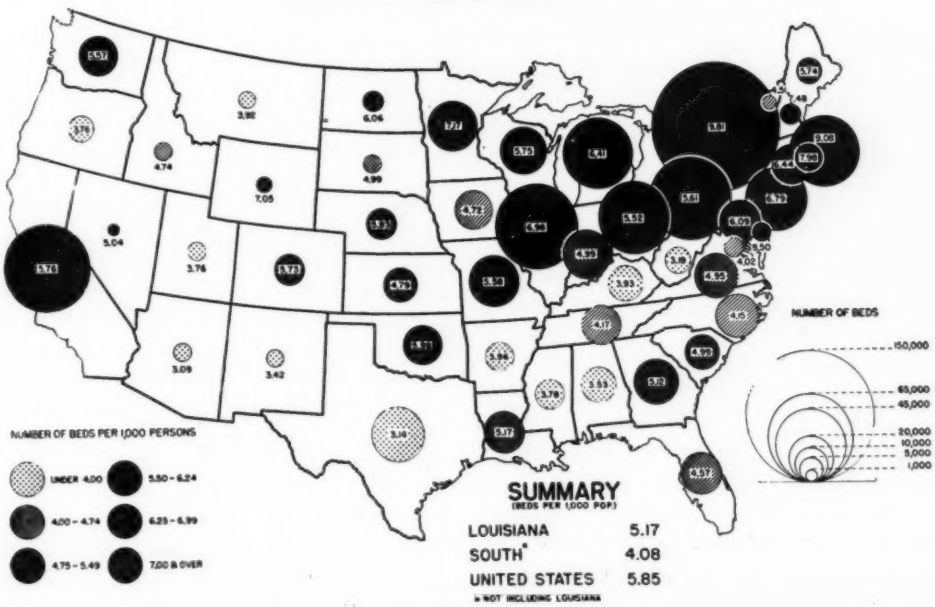

Figure 4

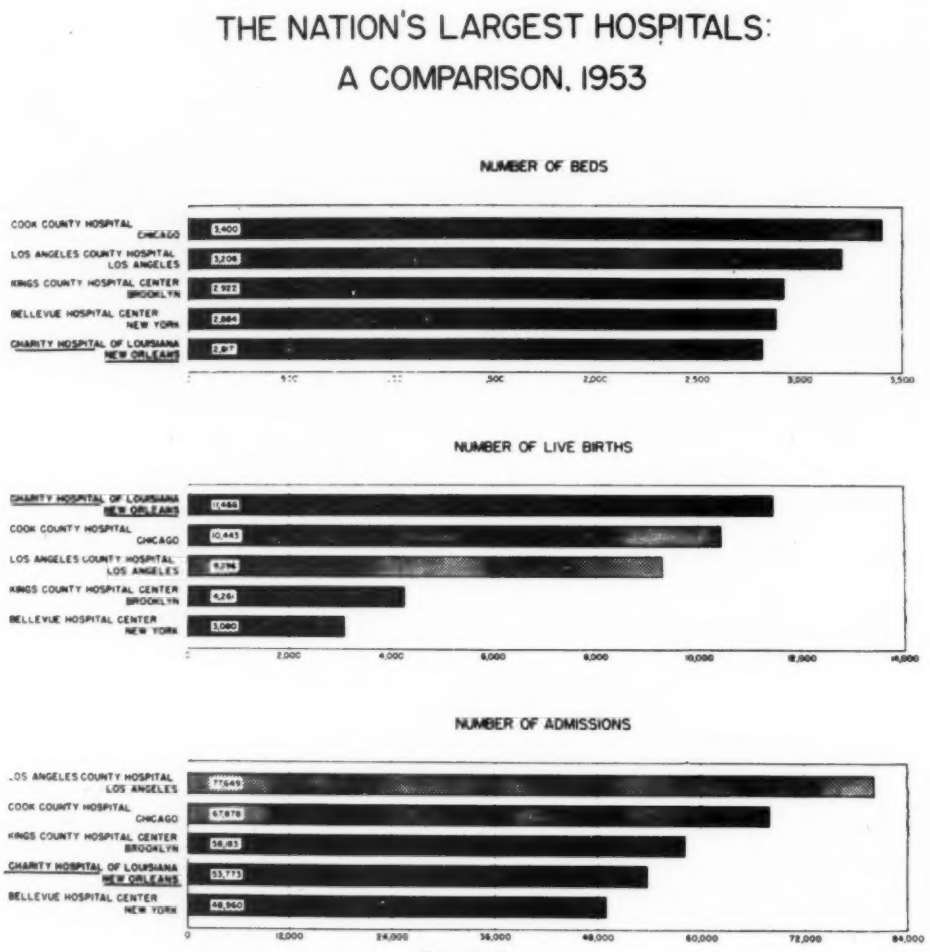

Figure 5

Southern States but stands a little below the national average.

The nation's five largest hospitals are compared graphically in Figure 5. Using the three indices shown, Charity Hospital at New Orleans ranks fifth, first, and fourth among these giant institutions. One of the reasons why New Orleans is among the leading medical centers of the United States is that the large numbers of patients of Charity Hospital comprise a reservoir of clinical medical material of great importance in medical teaching and research.

The last chart, Figure 6, shows number and proportion of all hospital beds in the state.

SUMMARY

Louisiana has a higher ratio of hospital beds per thousand persons of population than its neighboring Southern States, and it is about at the national average for hospital facilities. In 1953, there were 12,844 general, 9,527 mental, and 531 tuberculosis hospital beds in this state, a total of 22,902 beds of all types. The largest state hospital, Charity Hospital at New Orleans, ranks with the five largest in the United States in size.

HOSPITAL BEDS. BY TYPE.
LOUISIANA. 1953

TOTAL BEDS	22,902
GENERAL	12,844
NERVOUS & MENTAL	9,527
TUBERCULAR	531

Figure 6

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AN ACCOUNT OF THE EARLY HISTORY OF CESAREAN SECTION IN THE UNITED STATES *†

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BALTIMORE, MD.

While the operation of cesarean section is one of the oldest in the history of medicine, its origin is concealed under the dark cloak of antiquity. It has been called the most important operation since it is the only one in which two lives are involved. Few surgical procedures have been the subject of such bitter controversy throughout history. The very definition of the operation caused dispute among early authors, many of whom included in the term cesarean the operations for the removal of the fetus from the abdominal cavity following rupture of the uterus, as well as that for abdominal pregnancy. R. P. Harris, of Philadelphia, the most prolific and productive early writer on the subject in America, wrote succinctly, in 1872, as follows: "I take the ground, that there is and can be but one operation truly 'Caesarean', and that is the ancient 'section', made through the abdominal and uterine walls for the purpose of removing the fetus, with the hope of saving the life of the mother, and if possible that of the child."

CESAREAN SECTION IN LOUISIANA

In the early accounts pertaining to cesarean section in this country one finds frequent mention of physicians of Louisiana. It seems fitting here to call attention to some of their contributions.

Harris was so impressed with the frequent and successful use of the operation in Louisiana that, in 1872, he wrote: "No State in the Union probably equals Louisiana in the number of Cesarean operations, their successful results, or the early period of their history. That the operation was performed a number of times with success in the early part of this century, prior to any of the cases I have here recorded, there is every reason to believe; in fact, it is highly probable that the Louisiana operations constitute a fifth of the whole credit of the Union".

Francis Prevost, of Donaldsonville, Louisiana, is credited by Williams, as being the first in this country to perform cesarean section twice upon the same individual; in fact he is said to have operated upon four occasions prior to 1830, losing but one of the mothers and none of the children. Williams also stated that J. A. Scudday, of Louisiana, operated successfully on the same patient in 1846 and 1849, saving the mother and both children.

Both Eastman and Young state that the first recorded instance in America of the use of uterine sutures in cesarean section was that reported by Warren Brickell, who was Professor of Obstetrics in the

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New Orleans School of Medicine. He advocated their use both in cesarean section and ruptured uterus in his lectures in 1856, but did not put his idea into practice until 1867 when he used silver wire sutures. The patient recovered.

In his paper on the contributions of frontier American surgeons to cesarean section, Eastman cited Harris' report which, in 1871, insisted that the operation to be safe must be done early in labor. Harris based his thesis on the excellent reports from rural areas where it was known that the operations were performed in early labor while the patients were still in good condition. Especially creditable were the statistics reported from the plantations of Louisiana where the mortality from among the slave women was 12.5 per cent; while, in contrast, 75 per cent of the mothers died who were delivered by cesarean section in the City of New Orleans, where the operations were performed after many hours of labor, as was the usual custom in urban areas the country over.

In more modern times, your own C. Jeff Miller was one of the persistent and powerful voices on the very necessary side of conservatism in the use of cesarean section. According to Findley, about 1930, Miller wrote, "It is one of the paradoxes and one of the tragedies of medicine that certain measures designed primarily as life-saving and health-giving should carry in their abuse death and invalidism. Cesarean section is of this group. Originated for the salvation of the child and then of the mother, all too frequently it has become a death-dealing agent for them both".

THE FIRST CESAREAN SECTION IN THE UNITED STATES

In the first century, Plutarch, the great Greek biographer and moralist, said, "So very difficult a matter it is to trace and find out the truth of anything by history". This statement by the ancient writer is especially pertinent to any attempt to determine to which American physician belongs the credit of performing the first cesarean section. Of ten authorities consulted, six accord the honor to Jesse Bennett of Edom, Virginia, while four support John Lambert Richmond, of Newton, Ohio. From various sources we learn that Bennett, a country practitioner, was forced to operate upon his own wife. The consultant had tried forceps and had failed. Of the two choices, craniotomy or section, Mrs. Bennett chose the latter. The successful operation was performed on January 14, 1794; but it was not recorded for many years. On April 22, 1827, Richmond performed cesarean section upon a convulsive patient with a malformed vagina. The mother survived but the child died. This case was not reported until 1830. In the matter of chronology we are forced to conclude that Bennett deserves to be designated as the first physician in the United States to perform cesarean section. However, Richmond should share the credit since his case was the first recorded by a physician in this country.

Since Prevost, of your state, was credited with having performed four cesarean sections prior to 1830, it is possible that he may have antedated Bennett. However, this cannot be documented since Harris and S. M. Bemiss, of New Orleans, made a special search for the records of Prevost's cases to no avail.

THE FIRST USE OF UTERINE SUTURES IN THE UNITED STATES

According to Williams and Rucker, at Occuquan, in Fairfax County, Virginia, in June, 1828, an empirical physician performed a cesarean section and, for the first time in the United States and the second time in the history of the world, sutured the uterine incision. However, there is some question as to whether or not this operation was a true cesarean since some believe that, from the description, it was merely an operation for an old extra-uterine pregnancy. In any event, it is the first instance in this country in which sutures were used to close the uterus or the incision into an extra-uterine fetal sac.

Authorities seem to agree that Brickell's use of silver wire sutures to close the uterine incision following section, in 1867,

was the first recorded instance in America. Again, the luster of this "first" was somewhat dimmed when it was learned that Frank E. Polin, in Springfield, Kentucky, in December 1852, had successfully used silver wire sutures. Polin had 10 cases in which he used silver wires, saving five of the mothers; however, he did not record his series.

It is stated by Young, that J. Townsend, of New York, in 1867, used fine hemp as uterine sutures; and that T. A. Foster, of Maine, in 1870, employed silk for this purpose for the first time in the world.

Bennett is said to have used linen thread for the uterine sutures in his "first" cesarean. Adair stated that Curtin, in 1878, sutured the incised uterus with phenolized catgut — the first American operation in which animal material was used for sutures.

It is the opinion of Eastman that, "The conception and development of the silver wire suture in cesarean section was wholly an American achievement". Eastman further believed that the success of the early operations in this country in which uterine sutures were used, contributed significantly to the evolution of Sanger's hypothesis. In Sanger's monograph he acknowledged the work of his American predecessors, on the basis of whose statistics he demonstrated that the prognosis in cesarean section improved in relation to the number of uterine sutures used, particularly in those instances in which silver wire had been employed.

It was not until 1874, according to Young, that the peritoneum of the uterus was separately sutured. R. O. Engram, of Georgia, in performing cesarean section after craniotomy had failed, sutured the uterus with carbolized silk, using three deep sutures, three superficial, and four including only the peritoneum. The patient recovered. The case, however, was not reported until 1885. This is another example of a possible "first" having been lost by failure to report. Sanger's monograph appeared in 1882, and it is quite possible that Engram would have been given credit for contributing to Sanger's "multiple-layer" closure of the uterine wound.

CESAREAN SECTION EARLY IN LABOR

Perhaps the most significant contribution of American physicians in the history of cesarean section was the observation that the nearer to the onset of labor the operation was performed, the better was the prognosis for the mother and the baby.

W. P. Dewees, in 1832, and G. S. Bedford, in 1855, pointed out that, in their opinion, the alarming mortality following cesarean section in Great Britain and in certain instances in this country was due to the fact that the operation was used only as a matter of last resort. Dewees said, " . . . procrastination is the cause of the evil". It was suggested, if the operation was indicated, that it should be performed early in labor before the patient became exhausted.

In 1871, Harris insisted that the operation in early labor was the greatest factor in reducing mortality. It was the sheer weight of his collected data and his compelling writings which convinced the profession of the wisdom of what Eastman has called the "timely" cesarean operation. Kelly stated that Harris was the most prominent medical statistician the country had known. His writings were widely read in Great Britain and in Europe, and consisted in the main of six statistical surveys on the subject of cesarean section in this country. His data demonstrated the astonishing difference in maternal mortality when the operation was performed in early labor. Collected writings of Harris and others in 1881, as shown by Eastman, revealed that the maternal mortality in general for cesarean section in this country was 50 per cent; if the operation was performed within the first twenty-four hours of labor, 20 per cent; and following the operations done at the onset of labor, it reached the unbelievable level of below 10 per cent.

MISCELLANEOUS CONTRIBUTIONS

Phillip Syng Physick, Professor of Sur-

gery at the University of Pennsylvania, in 1822, suggested an extraperitoneal approach to the lower uterine segment by separating the peritoneal sac from the vault of the bladder. According to Williams, he antedated Baudelocque who was said to have described the same operation in 1823. However, these suggestions were not followed, and it was not until 1870 that T. Gaillard Thomas, of New York, performed the operation not knowing that it had been proposed nearly fifty years previously.

Many of the early repeat sections were performed in this country. Mention has been made of Prevost's four cases prior to 1830. Robert Estep of Columbiana County, Ohio, operated on the same patient in 1833 and 1834, and these are the first cases in this country of which there are accurate records. William Gibson, of Philadelphia, performed successful operations in 1835 and 1837; while J. A. Scudday, of Thibodaux, Louisiana, operated with success in 1846 and 1849 upon the same patient.

While Denman in Great Britain was among the first to cast doubt on the propriety of repeated craniotomies performed on the same patient with contracted pelvis, Meigs, of Philadelphia, in 1835, supported this view and was one of the first to act on it in his own country by advocating the cesarean operation in such instances.

Professor Porro, of Pavia, Italy, in 1876, first performed the operation which later bore his name. However, he was not the first to remove the gravid uterus in a living patient. In 1869, Horatio Storer, of Boston, did this as an emergency procedure because of uncontrollable hemorrhage encountered during a cesarean section on a patient with a fibrocystic tumor of the uterus. The patient had been in obstructed labor for three days, and she died about two days later. The fetus was macerated.

A controversy which has continued to this day, involved the employment of cesarean section in the treatment of placenta previa. Lawson Tait, of Birmingham, England, first suggested this in 1890, but did not perform such an operation until 1898. According to Young, Hutson Ford, in 1892, was the first in America to suggest this use of the cesarean operation. Young further stated, "In 1893, the first successful Caesarean section for placenta previa was performed by an American surgeon, A. C. Bernays". Prior to Tait's successful case in 1898, section had been performed for placenta previa three times in the United States. As late as 1930, J. Whitridge Williams and J. M. H. Rowland, of Baltimore, professors of obstetrics at Johns Hopkins University School of Medicine, and the University of Maryland School of Medicine, respectively, differed in their views regarding the use of cesarean section in treating placenta previa. The former believed that the operation was rarely indicated, while the latter advocated its more frequent use.

Among the chief proponents of the lower uterine segment section in this country were A. C. Beck, and J. B. De Lee. Each contributed modifications of the operation in 1919 and 1925, respectively. Together, they popularized the operation. De Lee is credited with coining the descriptive term "Laparotrachelotomy", in 1922.

As the incidence of cesarean section increased after the turn of the century, important American obstetricians inveighed against its misuse. Together, they constituted the voice of necessary conservatism. J. Whitridge Williams spoke of the "Furor Operativus" of obstetricians and general surgeons. Such other outstanding men in our field as F. S. Newell, R. W. Holmes, C. Jeff Miller, F. S. Kellogg, and Palmer Findley, to mention only a few, spoke and wrote against the indiscriminate use of the operation then in vogue throughout the world.

It seems fitting to close this discussion with a prophecy by R. P. Harris who contributed so much to the history of cesarean section in this country by his statistical writings, and his advocacy of the so-called "timely" section. In 1881, he wrote: "My own belief is, that in time the Cesar-

ean operation will be much more frequently performed than it has been, and with much better results, and that craniotomy will correspondingly diminish in favor as an elective expedient."

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MANAGEMENT OF CONSTIPATION DURING PREGNANCY

USE OF DIOCTYL SODIUM SULFOSUCCINATE IN 28 PATIENTS

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Constipation is a frequent complaint during pregnancy. If the condition is a result of the pregnancy itself, it usually can be successfully managed by proper control of diet, fluid intake, and exercise. Therapeutic measures are rarely required.

On the other hand, a number of patients give a history of some degree of chronic constipation prior to their pregnancy. In these the condition is apt to become more severe as pregnancy proceeds, and management is more difficult. Constipation is particularly severe during the third trimester when compression of the colon due to pressure in the abdominal cavity is probably a factor in causing atonicity.[2, 9]

In the latter situation, therapeutic measures are frequently necessary even though they may not be desirable. Administration of mineral oil during the period of time required may interfere with vitamin absorption during a most undesirable time. Laxatives are usually not advisable because of the congestion which they may produce in the pelvic region and because their effect is only temporary. Such mild cathartics as cascara or milk of magnesia have been most widely used [7] but any agent that would promote bowel movement without laxation would offer real and significant advantages.

The recent introduction of dioctyl sodium sulfosuccinate ‡ as a fecal softening agent [3, 10] led us to investigate its use in the constipation of pregnancy. The action of this agent is confined to a reduction of surface tension in the intestinal tract, and it presents none of the disadvantages of

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‡ Dioctyl sodium sulfosuccinate was supplied as doxinate by Lloyd Brothers, Inc., Cincinnati, Ohio, in the form of 60 mg. soft gelatin capsules.

the traditional agents used in the management of constipation.

MATERIAL

Twenty-eight pregnant patients complaining of a significant degree of constipation were treated with doxinate (R). All were outpatients seen at the Clinic during a period of six months during 1956. Constipation was characterized by passage of abnormally hard stools and infrequent bowel movements varying from once every other day to once or twice a week.

Twelve of the 28 patients had chronic functional constipation requiring frequent use of laxatives, enemas, or suppositories. In 14 patients the condition was less severe with a history of fairly frequent episodes of constipation. In only 2 instances could the disorder be attributed directly to the pregnancy itself. No major gastrointestinal disease was apparent in any of these patients although fibroids were present in one patient and hemorrhoids in another. Over half (54 per cent) of the patients required medication at rather frequent intervals to obtain bowel movement.

Most of these patients were under our care for a period of time sufficient to attempt correction of their constipation by physiologic measures. Dietary modification, increased fluid intake, and regulated exercise were uniformly unsuccessful. Therapeutic measures were therefore used as an adjunct.

All patients received a daily dose of 180 mg. of doxinate (R) (one 60 mg. capsule after each meal) for an initial period. Dosage was subsequently increased or decreased as needed.

RESULTS

Treatment with doxinate (R) was initiated at different times in individual patients with respect to their pregnancy. Approximately equal numbers of the group received the drug for the first time during each trimester. Results showed that the time of initial treatment had little bearing on the results obtained, although it was observed that patients sometimes required an increased dosage during the third trimester.

This regimen of treatment was satisfactory in 21 of the 28 patients (75 per cent). Two patients were able to discontinue the routine use of doxinate (R), using it for a few days only when irregularity or hard stools became noticeable. Constipation was satisfactorily controlled in one patient with a dosage of only 60 mg. daily. One patient found it necessary to take 360 mg. (six capsules) daily during the final trimester to obtain a continued satisfactory response.

As would be expected, the response was poorer among patients with pre-existing chronic functional constipation who had previously relied upon cathartics and enemas. Five of the 12 patients falling in this category responded satisfactorily to a daily dosage of 180 mg. of doxinate (R), 5 required 360 mg., and 1 required 540 mg. One patient did not respond favorably to this medication.

Three patients continued to take doxinate (R) during the puerperium with good results, and the impression was gained that normal bowel activity was restored more satisfactorily in them than in those having conventional treatment.

Friedman,[4] Marks[6] and Antos[1] have pointed out that the use of a mild peristaltic stimulant as an adjunct to doxinate (R) therapy in patients with chronic functional constipation is advantageous. Some of these patients might well have received additional benefit if such combination treatment had been used on a withdrawal basis. However, the primary purpose of this investigation was to evaluate the effect of doxinate (R) as a possible means of avoiding laxation entirely. Accordingly, laxative measures were not used.

In patients benefitted by doxinate (R) bowel regularity usually was obtained within two weeks. Softening of the stools occurred in every patient although actual bowel movement did not always result. Nevertheless, 24 of the 28 patients (86 per cent) eventually experienced regular

bowel movements, usually of daily frequency.

In the patient with hemorrhoids the softened fecal mass resulted in less painful defecation. The frequency of anorectal complications in pregnant women [5, 8] suggests an advantage in the use of doxinate (R) in such patients.

In general, patients commented favorably on the convenience of administration of doxinate (R). The capsule is small and easily taken and is much more acceptable than large doses of liquid medicaments.

SUMMARY AND CONCLUSIONS

1. Dioctyl sodium sulfosuccinate (doxinate (R)), when used in conjunction with a proper physiologic regimen, was effective in relieving chronic functional constipation in 24 of 28 pregnant women.

2. A daily dosage of 180 mg. of doxinate (R) was effective in 75 per cent of the patients treated. These included cases of pre-existing chronic functional constipation and others in which the condition became progressively worse during pregnancy.

3. Doxinate (R) effectively softened the stools of all patients. It is a valuable adjunct in the management of constipation during pregnancy, offering advantages over traditional methods.

4. Neither side effects nor toxic symptoms were observed when this agent was administered.

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DEVELOPMENT OF A RADIOISOTOPE TRACER TEST FOR THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE

(THE ROSE BENGAL I 131 HEPATOGRAM)*†

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INTRODUCTION

This paper is presented to describe recent progress in the development of an external tracer test (the Rose Bengal I 131 Hepatogram) for the direct measurement of liver vascularity, hepatic cell function, and bile flow interference. Our initial studies in 1954-55 [1, 2] indicated that the I^{131}-labeled Rose Bengal test had several advantages over indirect biochemical methods for evaluating liver cell damage. For example, the test may be performed repeatedly in patients with severe jaundice because of the minute doses of dye and radioactivity employed. Rose Bengal is handled specifically by the polygonal cells of the liver and not by the von Kupffer's cells.[1, 3] It is not reabsorbed from the intestines [1] and no reactions from tracer doses have been encountered in our experience [1, 2, 4] or that of others.[4-8]

In normal rabbits [1, 2, 4] and in human subjects the test has given reproducible results.[1-8] The liver uptake-excretion patterns from patients with acute hepatitis were distinctly different from normal during active phases and returned to normal patterns at the time of recovery.[1, 2, 4-8] Patients with advanced cirrhosis have

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shown grossly impaired liver uptake and excretion rates as well as distinctly diminished liver vascularity.[1, 2, 4] Test results in animals and man both have correlated well with the pathologic findings and also with the results of various biochemical liver tests.[1]

Liver uptake-excretion tracings from animals with surgically ligated common bile ducts indicated that acute complete biliary tract obstruction in man could be detected rapidly.[1, 2, 4] However, in clinical practice *acute complete* bile duct obstruction is a rarity. Most lesions interfering with the flow of bile cause either a gradually increasing degree of partial obstruction or an intermittent disturbance.[9-12] Tumors of the head of the pancreas and of the ampulla of Vater or stricture of the sphincter of Oddi are examples of lesions which frequently cause gradually increasing obstruction.[11, 12] Inflammatory lesions of the biliary canaliculi are known to produce acute obstructive jaundice.[13-16] Such lesions are probably caused by sensitization reactions following the administration of three main drugs—thorazine, methyl testosterone and arsphenamine [17, 18] —or by ascending bacterial infections. Thorazine jaundice has been confused with other types of obstructive jaundice previously described and several patients have been inadvertently treated surgically.[16] Fortunately, in most cases of thorazine reactions jaundice is transitory and biliary obstruction is incomplete.[13-16] However, in the rare severe forms there are periods during the course of the disease in which almost total obstruction may exist for several days.

The purpose of this paper is to demonstrate the usefulness of the Rose Bengal I ^{131} Hepatogram as an aid in distinguishing between polygonal cell injury and bile flow interference, particularly in patients in whom there is a problem in deciding between continued medical management and surgical intervention.

Recent laboratory studies in rabbits are presented to demonstrate the effects of biliary obstruction on polygonal cell function, the influence of agents causing liver stress on sensitizing the Rose Bengal Hepatogram, and the alteration of bile flow rates by drugs acting on the liver capillaries and hepatic cells. Recent clinical work has included the development of a modified test procedure designed to provide the information needed to distinguish between medical and surgical jaundice. Results in patients with total obstruction demonstrate its immediate differential diagnostic value. Its usefulness in evaluating liver injury and bile flow interference in patients with partial or intermittent biliary obstruction is presented. Repeated Rose Bengal I ^{131} Hepatograms in such patients may reveal the pathophysiologic nature of the primary lesion more quickly than indirect biochemical liver tests.

MATERIAL AND EQUIPMENT

A. *Radioactive Rose Bengal*: The Rose Bengal used (C.I. 779) is made radioactive by a procedure utilizing ion exchange reactions, giving a dye with high specific activity, that is, about 1 mc. per mg. The Rose Bengal I ^{131} is supplied commercially * in a sterile solution containing 10 mg. of dye and about 10 mc. of I ^{131} per ml. Samples used for test purposes are prepared to contain 5 microcurie per ml. by making suitable dilutions of the stock dye solution in normal saline.

B. *Gamma-ray Counting and Recording Equipment*: Gamma-ray activity is measured using a lead collimated scintillation counter (1 to 1½ inch sodium iodide crystal) connected through a combination rate-meter-scaler to an Esterline-Angus recorder (Fig. 1).

PRINCIPLES AND TECHNIQUES FOR PERFORMING RADIOACTIVE ROSE BENGAL I ^{131} LIVER FUNCTION TESTS

A. *Principles*:

1. *Physical*: The physical principles are based on the phenomenon that each gamma ray emitted by an atom of I ^{131} absorbed by the sodium iodide crystal within the detector causes a flicker of light. This light impulse is converted to an electrical

* Radioisotope Division of Abbott Laboratories, Oak Ridge, Tennessee.

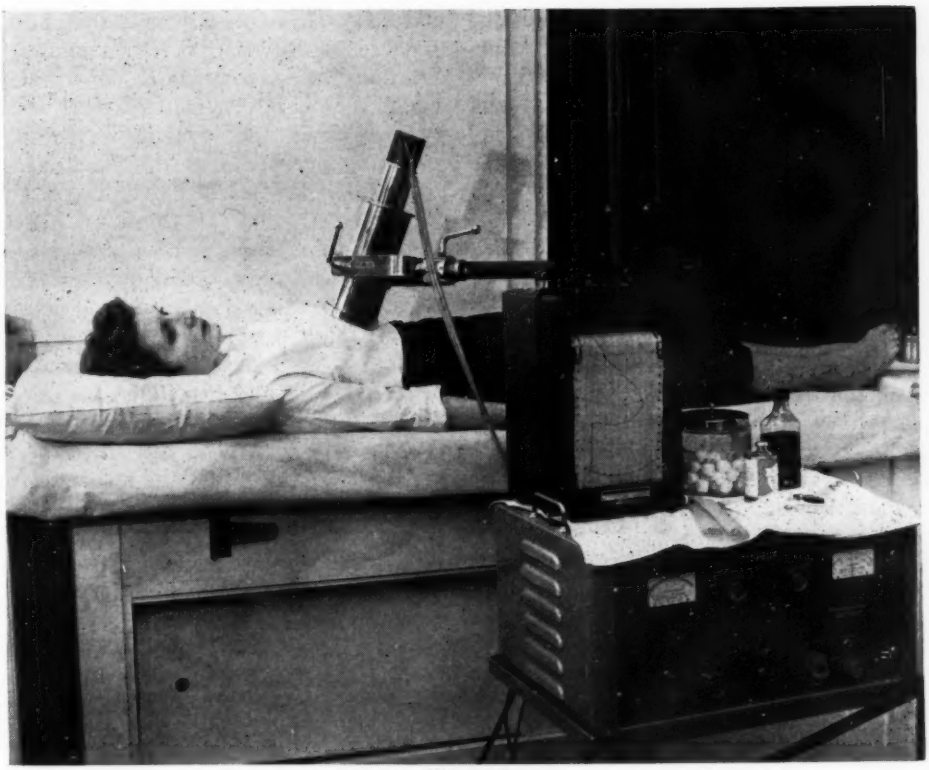

Figure 1

pulse within the photomultiplier tube and passes through several stages of amplification. The ratemeter measures the overall charge built up by the series of pulses which is proportional to the rate of gamma-ray emission. The levels of radioactivity following injection are recorded against time, showing the rates of accumulation and excretion of radioisotope in the organ. External measurements of blood clearance rates of I^{131}-labeled Rose Bengal reflect with sufficient accuracy the actual clearance values ordinarily obtained by blood-sampling techniques.[4]

2. *Physiological*: Following intravenous injection, Rose Bengal, a fluorescien derivative dye, is selectively absorbed by the polygonal cells of the liver[3] and excreted with the bile into the intestine, similarly to bromsulphalein. Substitution of gamma ray-emitting iodine ^{131} for the nonradioactive iodine atoms present in this dye permits *external* measurement of its uptake by the liver and excretion through the biliary tract, using gamma-ray scintillation detectors. Similar external blood clearance measurements made over the head, chest, or thigh give further data on liver function, indirectly.[19]

B. *Test Procedures*:

1. Originally, liver uptake and biliary excretion rates were measured by placing a lead-shielded scintillation counter over the upper anterior portion of the liver with the sensitive element (sodium iodide crystal) retracted 6″ into the lead shield to provide collimation.[1] The patient remained in a reclining position for the duration of the test (sixty to ninety minutes). The dose of dye varied between 0.2 and 5.0 mg., but the amount of radioactivity was held constant at 5 microcuries. The test dose (from 2-5 ml.) was injected intravenously at the rate of approximately 0.1 ml. per sec. The changing levels of radioactivity over the liver area were

transmitted from the counter through the ratemeter and registered on an Esterline-Angus recorder, giving a permanent record of the liver uptake-excretion pattern.

2. The abbreviated technique employed originally [2] to evaluate liver function was performed in a similar manner except that the rates of Rose Bengal liver uptake were recorded for only twelve to fifteen minutes during the almost linear phase, when negligible amounts of dye are being excreted. With the use of radioiodinated serum albumin (RISA) it was demonstrated that the initial leg of the Rose Bengal liver uptake curve provided an index of total liver vascular capacity. It was found that there is an extremely rapid rise in radioactivity in the liver, reaching a peak level in thirty to ninety seconds, followed by a slow steady rise for the next ten to fifteen minutes. By injecting RISA and recording similar measurements over the liver there is an identical rapid liver uptake for the first thirty to ninety seconds followed by a plateau level which remains constant for more than an hour. Since albumin remains in the circulation and is not specifically removed by the liver cells, as is the case with Rose Bengal, the height of the *initial* liver uptake segment of both curves appears to represent the amount of radioactivity in liver blood; hence it is evident that the first and second segments of the Rose Bengal liver uptake curves provide indices of total liver blood supply or vascular capacity, as well as of polygonal cell function.

Extensive studies in animals [4] have shown that the rates of liver uptake and blood clearance have a reciprocal relationship and the curves of uptake versus blood clearance are nearly mirror images. Recent investigations in patients as well as in rabbits have demonstrated that the rates of liver uptake-excretion, blood clearance and increases in the levels of upper intestinal radioactivity can be measured externally with a single scintillation counter.

3. The new clinical test procedure employs the same equipment used for standard I ^{131} thyroid diagnosis, that is, a collimated scintillation detector and a combination ratemeter-scaler, which may be connected to an Esterline-Angus recorder if so desired. The patient is placed in a reclining position and the exact areas to be counted are marked over the liver, the midabdomen and the thigh or head. To obtain data from which liver uptake-excretion and blood clearance curves may be plotted, the patient is given an intravenous injection (1 microcurie per 15 kg.) of the Rose Bengal I ^{131}, and counts are made initially over the liver for one minute beginning thirty seconds after the injection. The counter is shifted to the thigh and then to the mid-abdomen and similar one-minute counts are made. These three measurements are repeated as frequently as possible during the next thirty to forty-five minutes. Additional counts are made over the same areas for longer periods if the maximum liver level is not reached during this time. The patient is requested to return for repetition of the same three measurements at two to four hours and again in approximately twenty-four hours. When these data are corrected for background radioactivity, plots may be prepared which show the rates of blood clearance, liver uptake-excretion and delivery of dye to the upper intestinal tract (the Rose Bengal I ^{131} Hepatogram).

C. *Results of Animal Studies*:

1. *Common Bile Duct Obstruction*: Forty-two normal rabbits were tested with the Rose Bengal I ^{131} liver uptake-excretion blood clearance procedures using continuous recording techniques and duplicate equipment similar to that employed clinically. These animals were then placed in metabolism cages to measure urinary and fecal excretion of Rose Bengal for seventy-two hours. At twenty-four hours, external counts of radioactivity were made over their livers and mid-abdomens.

One week later groups of these controls were operated and their common bile ducts were ligated. Animals with common duct obstruction were then studied in the same manner as during the control period to

determine the effects of bile duct ligation on polygonal cell function and on urinary and fecal excretion of Rose Bengal. Data presented in Table I show that ligation of the common bile duct causes a rapid de-

TABLE 1

ROSE BENGAL I^{131} BILIARY OBSTRUCTION STUDIES IN RABBITS

DAYS OBSTR.	ANIMAL NUMBER	LIVER VASC. c/m/cm	LIVER MAX. c/m/cm	LIVER MAX / LIVER VASC.	$LET_{\frac{1}{2}}$	$LET_{\frac{1}{2}}$ / $LUT_{\frac{1}{2}}$	LIVER AND 24 Hours	% 48 EXCRETION 30 Hours URINE	% 48 EXCRETION 30 Hours FECES
0	6.2 CONTROLS	688 (375 - 880)	1376 (825 - 1890)	2.1 (1.5 - 3.0)	30' (17-60)	2.0 (1.1 - 3.7)	0.27 (0.1 - 0.48)	1.2 (0.4 - 2.6)	5.1 (1.8 - 6.7)
1	17	715	1425	2.0	62'	4.2	0.5	0.8	0.5
1	18	428	428	1.0	∞	∞	2.6	1.0	3.5
2	35	585	1050	1.8	∞	∞	1.1	—	—
2	36	800	1460	1.2	∞	∞	1.1	2.8	0.3
2	38	845	940	1.1	∞	∞	0.8	4.5	0.0
2	47	774	845	1.1	∞	∞	5.9	0.4	0.4
2	48	387	700	1.8	64'	4.3	0.8	0.1	0.5
5	2	572	750	1.3	210'	14.0	0.9	1.5	2.4
5	5	606	767	1.3	43'	2.9	1.0	1.1	2.2
5	37	980	1120	1.2	∞	∞	1.4	14.1	0.1
5	40	762	881	1.3	∞	∞	—	—	—
5	42	890	834	1.0	280'	18.3	1.4	1.0	1.8

terioration of liver function, as indicated by reductions in the rates of liver uptake and by decreases in the ratios of maximum liver uptake to vascularity level. It is apparent from the table that a few of the animals had incomplete biliary obstruction, which is evident from the near normal liver excretion rates and from the amounts of radioactivity found in fecal specimens. At necroscopy these animals were found to have either incomplete ligation with bile leakage or rupture of the gallbladder with localized chemical peritonitis and little liver injury. These experiments also showed that common duct ligation has a tendency to increase the small amount (1 to 2 per cent) of Rose Bengal normally excreted in the urine; however, the findings were so variable that it is unlikely that measurement of urinary excretion of Rose Bengal in patients with obstructive jaundice would provide data of diagnostic value.

2. *Bile Flow Rate Studies*: The rate of bile flow measured in normal animals by cannulation of the common bile duct was found to be relatively constant (0.05 ml. per min.) over periods of sixty to one hundred and eighty minutes. The influence of various drugs was tested simply by observing any alteration in the dropwise rate of bile flow. Epinephrine causes an immediate two- to three-fold reduction in rate, whereas decholin increases the bile flow temporarily by factors of five- to tenfold. Additional studies of this type to determine whether external liver measurements of radioactive Rose Bengal correlated with bile flow showed a parallel relationship between the externally detected radioactivity and that measured in bile samples.[4] Furthermore, the injection of decholin causes a sharp increase in bile flow, as indicated by an abrupt change in the slope of the external excretion curve which coincides with a rapid increase in the rate of bile flow seen visibly from the biliary cannula. In similar experiments this increase in bile flow rate by decholin could be accented by previous administration of epinephrine.[19] These laboratory findings suggest that a clinical test could be developed to indicate the patency of the upper biliary passages. It could be useful in studying patients with partial obstruction from acute biliary canaliculitis or cholangiolitis.

3. *Stress Testing*: It is generally recognized that indirect biochemical liver tests are relatively insensitive.[9, 20] Also, test procedures which do not place a load on the liver may fail to detect functional impairment because of the tremendous reserve capacity of the liver and its ability to regenerate rapidly.[21, 22] Therefore various physiological agents were injected prior to and in conjunction with Rose Bengal I^{131} testing. The material which has been shown to provide a practical method for stressing the polygonal cells is bromsulphalein. When this dye is injected five to forty-five minutes prior to Rose Bengal it requires doses up to 20 times the standard dose of 5 mg. per kg. before there is any alteration in the dynamics of Rose Bengal liver uptake-excretion. However, when 10 mg. doses per kilo. of bromsulphalein are mixed with tracer doses of Rose Bengal and given simultaneously, the dynamics of Rose Bengal liver uptake and blood clearance are altered only slightly (10 to 20 per cent) in normal animals (Fig. 2), but in animals recovering from carbon tetra-

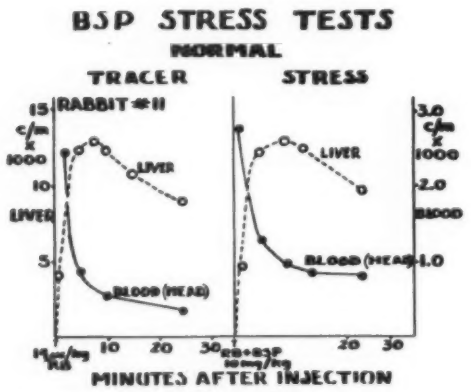

Figure 2

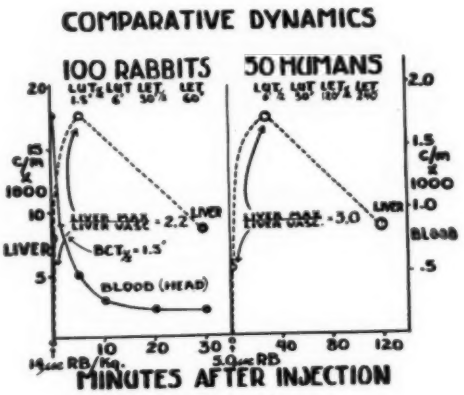

Figure 4

chloride poisoning this stress test is definitely positive (Fig. 3) when the tracer

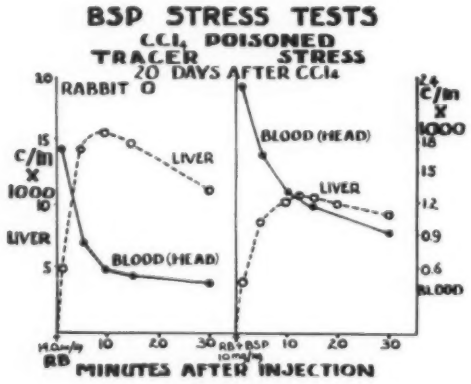

Figure 3

test has returned to normal. The BSP-RB I [131] stress test should have direct clinical application and also permit exact comparison of the relative sensitivity of the two dye methods in the same animal or patient simultaneously. Preliminary results indicate that this procedure should significantly increase the sensitivity of the Rose Bengal I [131] test in measuring polygonal cell injury of the liver.

D. *Comparative Dynamics in Man Versus Rabbits*: The information presented in Fig. 4 shows that the *average* liver uptake-excretion rates in 100 normal rabbits and 50 healthy human subjects are nearly identical except for timing. The liver uptake and blood clearance are about five times faster in rabbits than in man and the average excretion rate is four times faster. These temporal relationships render it possible to predict from controlled rabbit studies the disturbed physiology to be found in man.

E. *Clinical Results*: In all 50 of these normal healthy subjects standard biochemical liver tests have been almost entirely negative. An example of the normal relationships including blood clearance and the rate of delivery of Rose Bengal to the upper bowel is shown in Fig. 5. It is seen

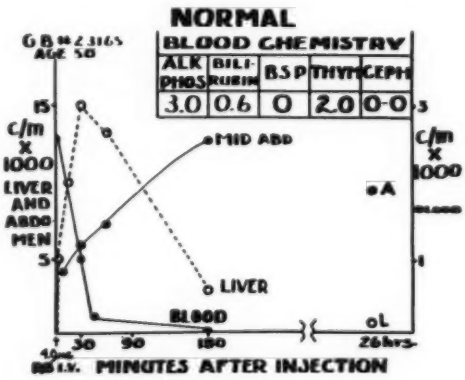

Figure 5

that the initial rise of activity over the liver (liver vascularity) is about 1200 counts per minute per microcurie of Rose Bengal administered, and that the subsequent rise of radioactivity in the liver reaches a maximum in approximately thirty minutes and then diminishes at a slower rate, reaching about 70 per cent clearance in three hours. The blood clear-

ance curve is practically a mirror image of the liver uptake curve. The blood is largely cleared by the time maximum liver uptake is achieved. From readings made over the mid-abdomen it is seen that Rose Bengal is being secreted with the bile into the upper intestinal area during the first thirty minutes and then excretion proceeds during the next two and a half hours at a rate similar to that of the decline in liver radioactivity.

1. *Acute Hepatitis*: In acute hepatitis the rate of liver uptake is grossly depressed during the acute phase of the disease and returns to normal over a period of weeks, as is shown in Fig. 6. Blood chemistry data presented in the same figure show the parallel relationship between the abbreviated Rose Bengal liver uptake test results and values from standard indirect biochemical liver tests.

2. *Chronic Hepatitis*: In chronic hepatitis the dynamics of liver uptake-excretion and blood clearance are also grossly depressed, and the biochemical liver tests

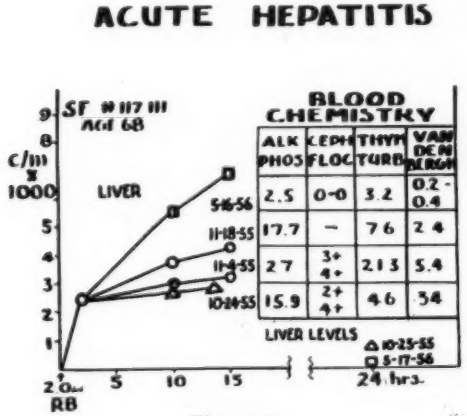

Figure 6

show impairment of several functions (Fig. 7). In this patient, blood clearance of Rose Bengal I [131] was measured by three methods simultaneously: (1) by continuous external recording of radioactivity counted over the top of the head, (2) by repeated external counts made over the thigh, and (3) by analyzing serial blood samples in a well scintillation counter. There is excellent agreement between val-

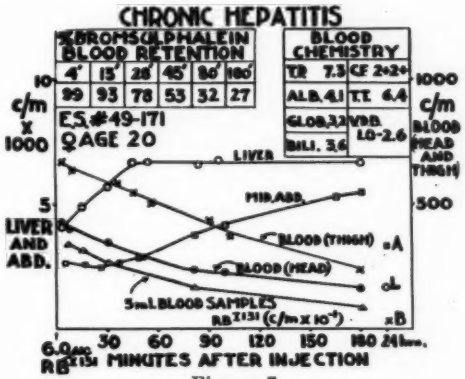

Figure 7

ues obtained from counting blood samples and continuously recorded radioactivity levels over the head and satisfactory correlation with repeated thigh counts. A 0.5 mm. lead shield was employed in the probe used for continuous head counting, to reduce low-energy scattered radiations. The blood retention of BSP given simultaneously was 53 per cent at forty-five minutes and 27 per cent at three hours.

3. *Complete Obstruction*: In patients with complete biliary obstruction from cancer of the head of the pancreas there is an associated liver cell impairment as indicated by the slow rates of liver uptake and blood clearance. Complete obstruction is demonstrated by total retention of dye in the liver at twenty-four hours and by no increase in abdominal radioactivity during the same time (Fig. 8).

4. *Complete Versus Partial Obstruction*: The differences between complete

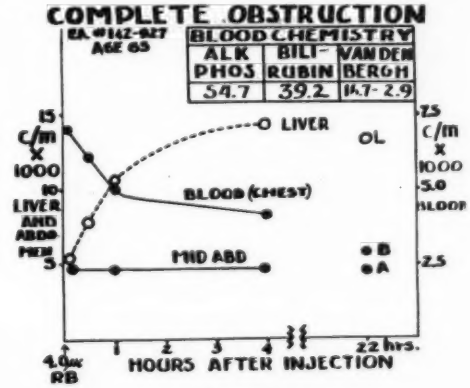

Figure 8

and partial biliary obstruction in respect to liver uptake-excretion curves alone are shown in Fig. 9. In cases of partial ob-

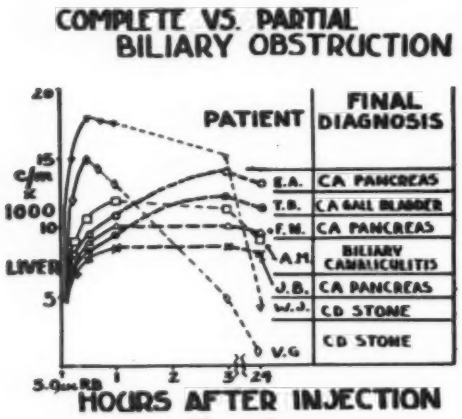

Figure 9

struction there are significant decreases in liver activity by three hours as compared with their maximum uptake values and extremely sharp reductions between the three and twenty-four hour liver levels. Furthermore, it is seen from these data that in partial obstruction cases the initial liver uptake rates are within relatively normal limits, whereas in patients with long-term high-level biliary obstruction there is an associated gross impairment of liver cell function, as manifested by marked reductions in rates of Rose Bengal liver uptake. Patient A. M. is an example of severe jaundice from intrahepatic biliary obstruction. He was treated surgically and explored for common duct stones. None were found at operation and the gallbladder, pancreas, and ampulla all appeared normal. Liver biopsy showed changes in the biliary canaliculi and around the central lobular areas similar to those found in obstructive jaundice from thorazine or methyl testosterone. His single Hepatogram showed moderate parenchymal damage and high-level biliary obstruction which was not quite complete.

5. *Case Report of a Typical Diagnostic Problem*: The problem of differentiating parenchymal liver cell disease from biliary tract obstruction is a difficult one because there is nearly always secondary polygonal cell injury in such cases. Biochemical tests for polygonal cell disease may be positive, as well as those which indicate biliary obstruction. Hepatograms presented in Figs. 10 to 13 were obtained from one individual wherein such a diagnostic problem existed. The patient (a 28-year-old woman) had been operated for chronic cholelithiasis and acute common duct obstruction from stone three months before the present admission. Data in Fig. 10

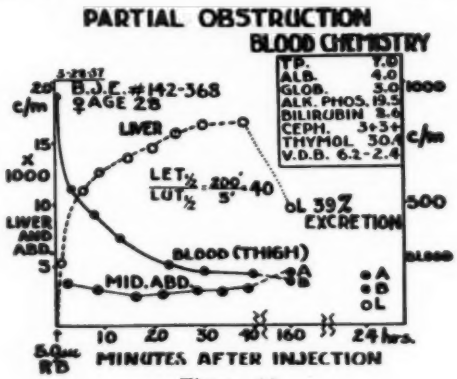

Figure 10

were obtained three days after the second admission. The patient had had signs and symptoms of an obstructive type of jaundice for three days prior to this admission. She had a sudden recurrence of right upper quadrant pain, nausea, vomiting, chills and fever, increasing jaundice, dark-colored urine and light-colored stools. The dynamics of her first Rose Bengal I 131 liver uptake-excretion curves (Fig. 10) indicated partial biliary obstruction but relatively little impairment of liver function. Blood chemistry showed a high serum bilirubin, a moderately elevated alkaline phosphatase, and positive tests for polygonal cell damage, as well as a positive direct-acting van den Bergh's reaction. Four days later the Rose Bengal I 131 Hepatogram was repeated (Fig. 11), at which time the patient was comfortable and less jaundiced and the Hepatogram showed a striking improvement in biliary excretion when comparison was made with the first test. However, there was a rise in alkaline phosphatase, along with a fall in serum bilirubin. A third Hepatogram was per-

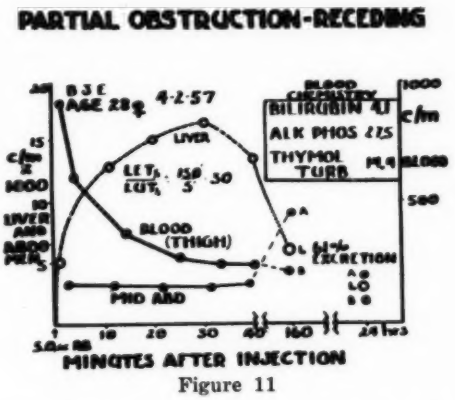

Figure 11

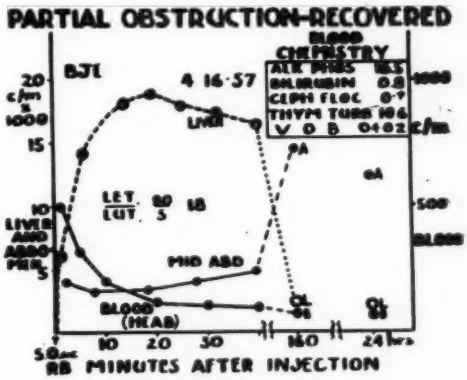

Figure 13

formed one week later (Fig. 12), at which time the dynamics had returned to entirely normal limits. However, the alkaline phosphatase showed a further increase. Clinically the patient was greatly improved, only mildly jaundiced, and had no significant abdominal complaints. Other biochemical liver tests showed improvement but remained definitely positive. A

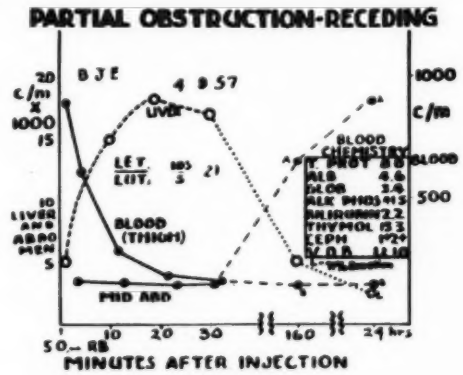

Figure 12

fourth Hepatogram was performed one week later (Fig. 13) and the findings again were entirely within normal limits and the patient had remained asymptomatic. Biochemical liver tests showed a further return towards normal values; however, the alkaline phosphatase remained somewhat elevated.

The differential diagnostic problem involved consideration of homologous serum jaundice because the patient had received blood transfusions during her recent operation three months previously; acute infectious hepatitis, because of her age; thorazine jaundice, because she was receiving psychiatric treatment, and a recurrence of her biliary tract disease on the possibility that all stones had not been removed at cholecystectomy and common duct exploration. The repeated Rose Bengal tests provided direct evidence in this case which indicated that neither homologous serum jaundice nor acute hepatitis was a likely cause because of the rapid changes in test results (days). In both of these primary liver diseases improvement in function occurs much more slowly (weeks). Results in this patient demonstrate the value of serial Hepatograms as an aid in distinguishing between primary liver cell injury and bile flow interference. In this individual it was apparent during the second Hepatogram that the most likely cause of her disease was a recurrent attack of common duct obstruction, from passing a stone. Furthermore, the repeated Hepatograms gave immediate information which was proved to be correct fourteen days later by standard indirect biochemical liver tests. The probable reason for the relatively slow response of biochemical tests is that these procedures give indirect indications of functional disorders within the liver and considerable time is required for readjustment to new equilibrium states.

DISCUSSION

In the differential diagnosis of medical versus surgical jaundice laboratory findings must be considered only as aids to

the clinical evaluation of the problem.[9, 14, 21] An accurate diagnosis may be made in the majority of patients without the use of laboratory tests. However, when clinical clues are either insufficient or give conflicting information, such cases present difficult diagnostic problems. Rapidly increasing painless jaundice in a patient having laboratory evidence of liver cell damage plus biliary obstruction is an example of a situation with which the physician is often confronted. Under such circumstances it is often necessary to decide between continued medical treatment and immediate operative procedures.[10-12] If the lesion is producing high-level biliary obstruction there is likely to be rapid deterioration of liver cell function. Each day of delay increases the operative risk and reduces the chances of recovery. On the other hand, if the lesion is either a widespread virus infection of the hepatic cells and/or intrahepatic inflammation of the fine bile passages, surgical procedures are detrimental and medical management is mandatory.[9, 13]

The data presented in this paper have shown that serial Rose Bengal I 131 Hepatograms may provide direct physiological evidence concerning the degree of bile flow interference as well as the relative amount of secondary liver cell injury in patients with partially obstructive jaundice. A gradually increasing degree of obstruction associated with slowly decreasing liver function over a period of several weeks is evidence favoring extrahepatic obstruction from cancer of the head of the pancreas, common bile duct stenosis or tumor of the ampulla of Vater.[9-12, 21, 22] Rapid changes in biliary patency occurring within a few days associated with only slight impairment of liver function favor the presence of ball valve common duct stone lodged near the ampulla.[21, 22] Such rapid changes in biliary obstruction are seldom found among patients with virus hepatitis of either of the two common types.[9] Fulmonating hepatitis should show rapidly deteriorating liver function associated with relatively less bile flow disturbance.[9] Severe thorazine hepatitis or other forms of cholangiolitis may have periods of nearly total biliary closure, but such patients show relatively little liver damage and clinically run a surprisingly mild course in most instances.[9, 13-19]

Another diagnostic feature which is provided by the Rose Bengal I 131 Hepatogram in patients having almost complete biliary obstruction is the slow rate of blood clearance and the persistently high levels of dye retention in the liver. From both clinical and animal data these high blood levels appear to be caused by two main factors, namely, severe associated liver cell injury and continuing intrahepatic regurgitation of Rose Bengal with the bile into the general circulation. High blood levels of Rose Bengal or of bromsulphalein in severe obstructive jaundice have no differential diagnostic significance [9] unless there is evidence of greatly reduced biliary tract patency, because the rates of blood clearance of both of these dyes are decreased in primary liver disease. However, a strongly positive bromsulphalein test or extremely slow blood clearance of Rose Bengal has about the same significance in respect to biliary obstruction as a strongly positive direct-acting van den Bergh's reaction. The latter test indicates intrahepatic vascular regurgitation of soluble bilirubin (solubilized by conjugation with glucuronic acid) during prior passage through the liver cells.[23]

The liver uptake of Rose Bengal I 131 is not prevented either by bilirubinemia or by high concentrations of bilirubin in the hepatic cells, as has been suggested by Brown and Glaser.[6] The damaged livers of severely jaundiced patients and heavily poisoned (carbon tetrachloride) rabbits have been shown to be capable of removing Rose Bengal I 131 from the circulation at rates proportional to their reduced liver function.[19] Furthermore, the livers of patients with partially obstructive lesions of the biliary tract have been demonstrated to be capable of completely removing Rose Bengal from the blood and excreting it

into the intestines. Furthermore, injection of pure bilirubin in amounts sufficient to increase the normal blood levels more than 100-fold has not altered the normal Rose Bengal I 131 liver dynamics in rabbits.[19]

The simultaneous injection of bromsulphalein at a dose level of 5 mg. per kg. along with tracer doses of Rose Bengal I 131 stresses the liver and decreases the rate of Rose Bengal blood clearance only slightly. However, there is no interference with the normal rate of bromsulphalein blood clearance. Larger stress doses of bromsulphalein (10 to 50 mg. per kg.) grossly depress Rose Bengal blood clearance and liver uptake rates.[19] Use of a mixture of bromsulphalein (5 mg. per kg.) and a tracer dose of Rose Bengal I 131 promises to be a means for further sensitizing the present Rose Bengal I 131 Hepatogram. The combined test (stress test) permits further investigation of the comparative sensitivity of the two separate dye tests simultaneously under identical conditions in man and in animals. Preliminary laboratory data indicate that when the Rose Bengal I 131 bromsulphalein stress test is negative in animals recovering from acute carbon tetrachloride hepatitis, the pathological lesions have largely disappeared and tissue repair is practically complete.[19]

From the data available from studying more than 100 patients and several hundred rabbits, and from work of others,[5-8] the Rose Bengal I 131 Hepatogram as presently performed is a practical test procedure for evaluating liver vascularity, hepatic cell function, the degree of biliary tract patency and/or of bile flow interference. In difficult diagnostic cases repeated Hepatograms may provide clues concerning the primary nature of the illness more quickly than indirect biochemical liver tests.

SUMMARY

Recent progress in the development of an external liver tracer test (Rose Bengal I 131 Hepatogram) has been described. Results of single and repeated Hepatograms in patients and animals having a variety of liver-biliary tract disorders have been interpreted. When the Hepatogram is performed repeatedly on patients in whom the diagnosis is difficult to establish on clinical grounds, the changing pathophysiological events are reflected immediately by distinct alterations in the tracer test results. Serial Hepatograms have revealed the true nature of the primary functional derangement prior to confirmation by more slowly responding indirect biochemical liver tests.

Additional basic studies have shown that the Hepatogram may also indicate abnormalities in the patency of the biliary canaliculi immediately after an injection of decholin. Furthermore, recent laboratory work has shown that a mixture of bromsulphalein with Rose Bengal I 131 may further increase the sensitivity of the Hepatogram.

In conclusion, the Rose Bengal I 131 Hepatogram meets the basic requirements of a specific organ test. It measures liver vascularity, polygonal cell function, biliary tract patency and/or bile flow interference directly. It is performed externally using the same standard radiation detection equipment as routinely employed in I 131 uptake tests for thyroid diagnosis. Results are reproducible and normal subjects have characteristic Hepatograms which are distinctly different from those found in patients with a variety of hepatobiliary disorders. Serial test results correlate well with the clinical findings and indicate the underlying pathophysiological disturbances, before confirmation by standard biochemical liver tests. The Rose Bengal I 131 Hepatogram is presently the most sensitive specific test for polygonal cell function of the liver and is also of distinct value in the differential diagnosis of hepatobiliary disease.

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PROPOSED CHANGES IN THE MEDICAL AND LEGAL HANDLING OF NARCOTIC ADDICTION

In the last several years changes in the manner of medical and legal handling of narcotic addiction have been proposed. Articles have appeared in the lay press and in professional magazines, presentations have been made before subcommittees of Congress, and a resolution was presented to the House of Delegates of the American Medical Association, concerning certain phases of the problem, in June 1954. This resolution favored the legalization of distribution of narcotics to addicts under the following safeguards: (1) establishment of narcotic clinics in cities where needed, under the aegis of the Federal Bureau of Narcotics; (2) registration and fingerprinting of narcotic addicts; (3) keeping of accurate records; (4) administering optimal doses at regular intervals to addicts at cost, or free; (5) prevention of self-administration; (6) attempt cures through voluntary hospitalization, if possible; and (7) avoidance of forceful confinement.

Consideration of the problem of the handling of narcotics, as a whole, brings out two points of view, not entirely divergent in theory, but far apart in the practical handling of the problem. One point of view as expressed could be summarized with the statement that drug addiction should be treated as an illness and not a crime, as it is an expression of an emotional problem and should be approached psychiatrically. It is stated that drug addiction is "a health problem which needs police measures for adequate control," and that our laws have made more difficult the sane, effective management of addiction. It is proposed in this situation that medical, psychiatric, and social services be made available to addicts, and that the follow-up of these patients be entirely free of punitive aspects. It is recognized that psychiatric care is needed and that the matter is complex. It is stated that a great deal of benefit may be achieved when it is possible to adjust the environment in the patient's favor. It is proposed that mandatory minimum sentences be abolished. These proposals are advanced with a view that the amount of addiction would be decreased and that the plight of the addict would be made less hard.

The resolutions mentioned above, which were presented to the House of Delegates of the A.M.A. were thoroughly studied by reference committees, by the Board of Trustees, by the Council on Pharmacy and Chemistry, and by the Council on Mental Health through a committee on narcotic addiction. In the past two years this

committee has given detailed study to the matters presented and has rendered a comprehensive report to the A.M.A. with certain recommendations. The report is a valuable summary of the problem and considers the development of the medical and legal aspects of addiction from the time following the adoption of the Harrison antinarcotic law to the present. The report comments with some caution in regard to the establishment of clinics, and notes that the clinics set up between 1919 and 1923 were unsatisfactory; that there was some abuse of the clinics, but the extent of the abuse was indeterminable. As a reaction against the clinics, the medical profession played a major role in formulating the policy which led to the closing of these clinics, and it does not recommend the establishment of clinics for the purpose of supplying drugs to addicts. The report does recommend continued research on the problems of addiction and comments that one of the current difficulties in formulating adequate programs is the lack of knowledge which should be both basic and clinical. It recommends that the American Medical Association continue to study the narcotic laws with the view of further clarification of the rights and duties of physicians. It points out that the phrases in the current law "in the course of professional practice only" and "prescription" remain vague and confusing. It further recommends improvement in the care of addicts, which would include increase in institutional facilities, increase in the postinstitutional treatment of addicts. Civil commitment to institutions, rather than criminal is advised, and abolition of criminal sentences for addicts who are guilty only of illegally possessing and obtaining opiates, marijuana, and cocaine.

The report states that mandatory sentences for addict violators would interfere with the possible treatment and rehabilitation of addicts and that this could be abolished.

The Council recommended that the policy of voluntary admission for the treatment of addiction be continued, extended, and encouraged.

The House of Delegates of the American Medical Association approved the report and stated that the changes proposed in the legal handling of addicts should be undertaken cautiously so that we could progress realistically.

The national experience in the last forty years indicates the wisdom of the latter statement. Before the legal control of narcotics was established it is estimated that addicts were 1 in 400 in the general population, and they are now about 1 in 3000, giving us no more than 60,000 addicts. The states with the strictest laws have the least addiction.

Opiate addiction in itself does not appear to be an incentive to commit crime except for the purpose of securing the drug. This, however, is not true of cocaine and marijuana. It is estimated that 80 per cent of addicts are criminals first, and in general, become addicts in association with other addicts. The relapse rate continues high. In 1955, there were 3,724 admissions to the two federal narcotic hospitals. About two thirds of these were readmissions.

The medical profession, therefore, has before it the continuously revolving problem of narcotic addiction. The fate of 60,000 addicts is pitiable. What can be done to alleviate it should be done. It should not be undertaken at the risk of producing more addicts. Addiction is at its lowest point in the states that have the best law enforcement and reached its lowest point in years during the second world war when blockade was almost complete. Medical measures may possibly do much to lighten the burden of the unfortunate addict as an individual. In 80 per cent of addicts who were criminals before addiction developed, the illness phase of addiction is overshadowed by the criminal aspect. We would deduce, therefore, that any sharp relaxation of legal measures would have just the opposite effect to what the proposers of leniency are expecting.

ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

AMERICAN MEDICAL EDUCATION FOUNDATION

Within a reasonably short period of time every member of the Louisiana State Medical Society will be contacted by Dr. Edgar Hull, Chairman of the American Medical Education Foundation Committee, concerning a contribution during 1957.

The A.M.E.F. is an organization working among physicians, trying to interest said physicians in contributing toward non-federated medical education. No monies turned over to them or directly to a school or schools of choice are taxed for handling in any way. The A.M.E.F. is supported by the American Medical Association and this collection service is absorbed by the American Medical Association.

Statistics prove that in recent years, the A.M.E.F. has been poorly supported by physicians in Louisiana; considerably more money being given to L.S.U. and Tulane than was donated by our group.

In order for us to keep medical education in private hands, there must be some changes made. Without our support, the deficit incurred by medical schools each year is around ten million dollars.

I, personally, have been guilty of non-interest for several unjustifiable reasons, but my eyes have been opened and I can see the light—hence my appeal to you.

It is my hope that in 1957 we will break all records on the number of men contributing. Heretofore, a few have carried the ball and it would be considerably more fitting to have participation approximate one hundred per cent of our membership.

Please read the Chairman's letter and give considerable thought to an early contribution to the school or schools of your choice. There shall be committees from all of the congressional districts of the State, one of which may contact you. Please be receptive and make their work easy.

H. Ashton Thomas, M. D.
President
Louisiana State Medical Society

106th ANNUAL MEETING AMERICAN MEDICAL ASSOCIATION

The recent meeting of the American Medical Association held in New York will go down on record as the largest and one of the best to date.

The attendance broke all records. Total registration was 55,847, including 19,469 physicians. The next largest attendance was experienced at Atlantic City in 1947 when 15,667 physicians were registered and at the last Chicago meeting, there were 9,969 physicians in attendance.

Louisiana was well represented by over fifty of its physicians. Keep the attendance up. This is really a postgraduate program containing many subjects of interest, and more of our doctors should take advantage of this wonderful opportunity for learning.

Revision of the Principles of Medical Ethics, relations with the United Mine Workers of America Welfare and Retirement Fund, the federal government's Medicare Program, new standards for medical schools, a new statement of occupational health programs, and Social Security benefits for physicians were among the wide variety of subjects acted upon by the House of Delegates.

Dr. Gunnar Gundersen, La Crosse, Wis., member of the A.M.A. Board of Trustees since 1948 and chairman for the past two years, was unanimously chosen president-elect for the year ahead. Shortly after his election the Board of Trustees selected Dr. Edwin S. Hamilton of Kankakee as its chairman. Dr. Hamilton has been a Board member since 1948 and served in the House of Delegates for 10 years prior to that.

Other officers elected or re-elected were:

Dr. Jesse Hamer of Phoenix, Ariz., vice-president; Dr. George F. Lull of Chicago, secretary; Dr. J. J. Moore of Chicago, treasurer; Dr. E. Vincent Askey of Los Angeles, speaker, and Dr. Louis Orr of Orlando, Fla., vice speaker.

Four new members were elected to the Board of Trustees: Dr. George Fister of Ogden, Utah, to succeed Dr. James R. Reuling; Dr. Cleon Nafe of Indianapolis, Ind., to succeed Dr. James R. McVay; Dr. James Z. Appel of Lancaster, Pa., to replace the late Dr. Thomas P. Murdock, and Dr. Raymond McKeown of Coos Bay, Ore., to replace Dr. Gundersen.

The House voted the 1957 Distinguished Service Award to Dr. Tom Douglas Spies, director of the nutrition clinic, Hillman Hospital, Birmingham, for his outstanding contributions to the science of human nutrition. For only the third time in history, the House also voted a special citation to a layman for outstanding service in advancing the ideals of medicine and contributing to the public welfare. Recipient of the award was Henry Viscardi, Jr., West Hempstead, N. Y., founder and president of Abilities, Inc., which employs only severely disabled persons.

MEDICAL NEWS SECTION

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
Calcasieu	Fourth Tuesday every other month	Lake Charles
East Baton Rouge	Second Tuesday of every month	Baton Rouge
Morehouse	Third Tuesday of every month	Bastrop
Natchitoches	Second Tuesday of every month	
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of every month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Tangipahoa	Second and fourth Thursdays of every month	Indepencence
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

THE NEW ORLEANS GRADUATE MEDICAL ASSEMBLY ELECTS NEW OFFICERS FOR 1957 - 1958

The twenty-first annual meeting of The New Orleans Graduate Medical Assembly will be held March 3-6, 1958, headquarters at the Roosevelt Hotel.

The following officers and members of the Executive Committee have been elected for this year:

Dr. Charles L. Brown, President

Dr. J. O. Weilbaecher, Jr., President-elect

Dr. Max M. Green, First Vice-President

Dr. Joseph N. Ane, Second Vice-President

Dr. M. M. Hattaway, Third Vice-President

Dr. Maurice E. St. Martin, Secretary

Dr. Ralph M. Hartwell, Treasurer

Dr. V. Medd Henington, Director of Program

Dr. Sam Hobson, Assistant Director of Program

Dr. H. Reichard Kahle, Assistant Director of Program

Executive Committee

Dr. Eugene H. Countiss (retiring President)

Dr. Hugh T. Beacham

Dr. George D. Feldner

Dr. George H. Hauser

Dr. W. E. Kittredge

PAN-PACIFIC SURGICAL ASSOCIATION

Seventh Congress

The Seventh Congress of the Pan-Pacific Surgical Association will be held in Honolulu, Hawaii, November 14-22, 1957. All members of the profession are cordially invited to attend and are urged to make arrangements as soon as possible if they wish to be assured of adequate facilities.

An outstanding scientific program by leading surgeons with sessions in all divisions of surgery and related fields promises to be of interest to all doctors.

Further information and brochures may be obtained by writing to Dr. F. J. Pinkerton, Director of the Pan-Pacific Surgical Association, Room 230, Young Building, Honolulu, Hawaii.

BOOK REVIEWS

Textbook of Endocrinology; Edited by Robert H. Williams, 2d ed. (Multiple authors), Philadelphia, Pa., W. B. Saunders Company, 1955, 776 p. Price $13.00.

This is an interesting, outstanding volume on clinical endocrinology. It is well edited and organized. The chapter by Reifenstein will probably take the place of subsequent revisions of "The Parathyroid Gland and Metabolic Bone Disease" by Albright and Reifenstein (1948).

It would be difficult for the average internist to criticize this book.

FRED M. HUNTER, M. D.

PUBLICATIONS RECEIVED

Doubleday & Co., Inc., Garden City, N. Y.: A Woman Doctor Looks at Love and Life, by Dr. Marion Hilliard.

Duke University Press, Durham: The Compleat Pediatrician, by W. C. Davison, M. D., and Jeana Davison Levinthal, M. D., (7th edit.).

Grosset & Dunlap, Inc., N. Y.: A Visit to the Hospital, by Lester L. Coleman, M. D., with an introduction by Flanders Dunbar, M. D.

Grune & Stratton, Inc., N. Y.: Some Milestones in the History of Hematology, by Camille Dreyfus, M. D.